

ENCEPHALITIS LETHARGICA

and

A NOTE of other CASES very possibly
dependent upon the same PATHOLOGICAL

VIRUS

by

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INTRODUCTORY .

A picture of disease "in the making" is always an engrossing topic. Within the last twelve months, in common no doubt with other observers, the writer has met with numerous cases of a type with which he was previously unfamiliar. ENCEPHALITIS LETHARGICA, the name applied by VON ECONOMO to a "new disease" which made its appearance in Vienna in 1917, would seem to be applicable to cases observed in France and in this country during the past year. The incidence of a new disease which is evidently widespread, though but seldom recognised, which from the diversity of its clinical manifestations raises numerous problems in differential diagnosis, the morbid anatomy of which is in process of construction, the symptomatology of which calls for more precise elucidation, the etiology and pathology of which are still obscure, necessarily compels the attention of the Physician and arouses the interest of his more purely scientific confrère, the Pathologist. A Blue Book published under the auspices of the Local Government Board, in the late autumn of 1918, entitled "The Report of an Enquiry into an obscure Disease", constitutes/

constitutes, so far as the writer is aware, the only attempt to deal systematically with the subject of encephalitis lethargica. The recorded experience of an individual observer, although necessarily more limited in scope, may, it is generally acknowledged, elucidate aspects of a subject and indicate a sense of perspective which a collective Report fails to represent. This is advanced as an excuse, if one is necessary, for the presentation of the following record.

Clinical observation is as important as Pathological Research in the progress of practical medicine, a fact that is, at the present day, often lost sight of. At a time when no definite information is forthcoming as to the causation of a clinical entity, it is indeed to the Clinician that medicine looks for progress. In the present thesis, the writer proposes to discuss the subject of encephalitis lethargica. He lays no claim to the discovery of any startling fact, but he believes that his clinical observations and the conclusions derived from his personal experience will prove to be a definite addition to the existing state of knowledge on the subject.

THE PICTURE of ENCEPHALITIS in the EARLY FORTIES of LAST CENTURY.

The term "ENCEPHALITIS" employed in its widest sense is applicable to all inflammatory processes which affect the brain. As a preface to subsequent considerations, it is both interesting and instructive to trace the processes of elimination and evolution which have led up to present day pathological and clinical conceptions.

The views expressed in a remarkable book entitled "Diseases and Derangements of the Nervous System" by MARSHALL HALL, an authority whose name ⁽¹⁾ is to be remembered as one of the most distinguished of British Neurologists, and one of the pioneers of scientific medicine, which was published in 1841, may be accepted as indicating the last word upon the subject in the early forties of the Nineteenth Century.

This Author deals with diseases of the Brain in four chapters entitled as follows:-

- (1) Encephalitis:
- (2) Congestion and Haemorrhage:
- (3) Tumours, Hypertrophy and Atrophy: and
- (4) Mania and diseases resembling it.

of/

Of Encephalitis he writes:-

"Encephalitis must be distinguished into -

- (1) Inflammation of the Membranes and
- (2) Inflammation of the substance of the brain."

To the former he applies the term "Cerebral Meningitis", to the latter "Cerebral Myelitis". Regarding the etiology of encephalitis he says:-

"The causes of encephalitis are mechanical injuries of the head itself, blows, falls, contrecoups; excessive mental application, anxiety, etc.; the intemperate use of spirits; exposure to the sunbeams, etc. Frequently encephalitis forms a complication of other diseases of the system, or of distant organs, especially fevers, the exanthemata and dropsies. It is, also, frequently the effect of other diseases of the encephalon itself; it is excited round the coagulum, or cyst, in cases of cerebral haemorrhage, tumours, tubercles, etc. It is also sometimes excited by ossifications or projecting spiculae of bone. Meningitis and Myelitis frequently excite each other. Encephalitis is said to have followed the suppression of the catamenia and other discharges. It is sometimes connected with rheumatism".

Referring to the symptomatology, MARSHALL

HALL/

HALL enumerates a number of symptoms, which as we now know, are met with alike in meningitis, cerebral softenings and encephalitis, but he makes no attempt to differentiate between these various conditions. As regards diagnosis, he says:-

"There is no symptom perfectly diagnostic of
 "meningitis and myelitis. The former is more
 "marked by acute pain, delirium and convulsions;
 "the latter by muscular contraction, alternating
 "with, or followed by paralysis".

The views of the English master represent the state of knowledge at the time he writes. A perusal of his work indicates that at this time meningitis, cerebral softenings, abscess of the brain and non-suppurative encephalitis were not differentiated clinically, that it was not realised that cerebral softenings were commonly caused by vascular occlusion; that the various forms of meningitis were not distinguished from one another, either by the physician or on the post-mortem table; that the relationship of disease of the middle ear to abscess of the brain was not yet recognised; that etiological inferences were essentially based on crude clinical considerations and that localisation of function in the brain was still an unexplored field.

So much for the state of knowledge eighty years/

years ago. The writer has specially selected this period for comparative purposes, since this marks the time when the processes of elimination and evolution which have led up to the present conception of encephalitis may be said to have commenced.

THE PROCESSES of ELIMINATION which have
led up to the PRESENT DAY CONCEPTION of
ENCEPHALITIS.

A study of the works of the older writers demonstrates that the present day conception of encephalitis has been arrived at in part, by the exclusion of a variety of conditions, e.g., cerebral softenings, meningitis, and abscess of the brain, which have been proved to present a distinctive pathology and symptomatology, in part by a process of positive differentiation, whereby attempts have been made to establish positive entities or types presenting characteristic features. Let us glance, in the first instance, at what has been above referred to, as the process of elimination..

(2)

VIRCHOW'S epoch making work upon Embolism and Thrombosis, which was published in 1847, may be said to have opened a new field in medical science.

Very/

Very soon it was discovered that the great majority of the pathological lesions of the brain, which had been previously attributed to an inflammatory process were, in reality, due to a softening of the brain tissues, or encephalomalacia, a consequence of cutting off, of the blood supply. The credit for this great advance in cerebral pathology is undoubtedly due to VIRCHOW, for subsequent observers merely applied his principles to disease, as it affects the brain.

Again, as time went on, it became apparent that the inflammations of the membranes of the brain constitute a definite pathological entity, and that the associated inflammatory involvement of the brain substance was a secondary process, a consequence of anatomical propinquity. With the introduction of the (9) procedure of lumbar puncture by QUINCKE in 1891 and the application of cytological, chemical and bacteriological technique to the examination of the cerebrospinal fluid, great advances were made in the differential diagnosis of the varieties of meningitis.

A further step was reached when the relationship of otitis media, to abscess of the brain was recognised, for it then became possible to separate a large group of cases with a definite etiology and symptomatology. Although the writer has been unable to/

to ascertain definitely to whom the credit is due for the discovery of this relationship, he finds
 (3)
 that HUGHES BENNETT in his "Principles and Practice of Medicine" (1858 p.332) writing of cerebral abscess says:-

"Most of the cases I have seen have been in scrofulous subjects and more especially such as have laboured under some form of this connected with caries of the temporal bone - - - - but as regards diagnosis in reference to meningitis and cerebritis" (he uses the latter term as the equivalent of encephalitis and as including abscess) "we cannot separate them".

(10)
 MACEWEN'S great work on the pyogenic diseases of the brain and spinal cord (1893) was, beyond doubt, the means of establishing the general recognition of the association between otitis and abscess of the brain.

The field of encephalitis has, it will thus be seen, been very greatly restricted, since the time of MARSHALL HALL by the withdrawal of the cerebral softenings, of meningitis, and of intracranial abscess. Indeed, it may be said, that encephalitis is, or perhaps it would be more correct to say, has been in the past, one of the rarities of medical practice.

THE PICTURE of ENCEPHALITIS in the EARLY
NINETIES of last CENTURY.

As indicating the recognised place of encephalitis in the latter days of the last century, the writer proposes, in the next instance, to draw the attention of his reader to the second edition (11) of Sir WILLIAM GOWERS' Manual which was published in 1893, fifty years after the appearance of MARSHALL HALL'S work. GOWERS, who was one of England's greatest clinicians, was a great accumulator of knowledge. Probably no British Neurologist of his day had a wider acquaintance with continental literature. This author, in his exhaustive Text Book, devotes only five pages to the consideration of acute inflammation of the brain.

"Putting on one side the cerebral softenings
"and meningitis, the residual cases", he says,
"are not numerous. Acute inflammation of the
"brain usually results from one of three causes -
"a traumatic injury, contiguous inflammation, or
"some septic influence".

The information to be derived from GOWERS' description of the etiology and symptomatology of acute inflammation/

inflammation is vague and unsatisfactory, but it represents the state of knowledge at the time. Diagnosis is dismissed in two sentences, as follows:-

"In many cases the symptoms are identical
 "with those of meningitis over the corresponding
 "region of the brain. In the form that results
 "from specific blood states, the condition may be
 "suspected if cerebral symptoms become more pro-
 "nounced after the pyrexia, but our knowledge of
 "the effect of the lesions is still too meagre to
 "permit any definite diagnostic rules to be laid
 "down". Of prognosis and treatment GOWERS merely
 says:- "The prognosis of acute simple inflammation
 "of the brain as distinguished from that of the
 "membranes, can only be made from the severity of
 "the symptoms. Its treatment is, on the whole,
 "similar to that of inflammation of the membranes".

C O N S T R U C T I V E E V O L U T I O N

of

NON-SUPPURATIVE ENCEPHALITIS.

At the time GOWERS wrote, attempts had already been made to differentiate types of non-suppurative encephalitis.

VIRCHOW/

(4)

VIRCHOW in 1865 described what he regarded as a form of encephalitis occurring in the new-born infant. His views, however, have met with considerable criticism, and since VIRCHOW'S Encephalitis Neonatorum is a subject of purely pathological interest, it is unnecessary to do more than refer to it in this historical resumé.

(5)

WERNICKE in 1881 described in his Text Book, three cases of encephalitis, characterised clinically by an ophthalmoplegia of more or less sudden onset, and pathologically by an acute haemorrhagic inflammation of the grey matter of the floor of the third and fourth ventricles, and the neighbourhood of the aqueduct of Sylvius. Since the symptoms were purely motor, since the upper bulbopontine nuclei were affected, and since the process was an inflammatory one, he compared the condition to acute poliomyelitis and termed it Polioencephalitis Superior, a nomenclature which was, perhaps, unfortunate, since the two conditions are probably distinct.

(13)

MURAWIEFF, who in 1897 described two cases of acute haemorrhagic superior polioencephalitis, states that up to that time only some sixteen or seventeen cases in all had been recorded. According to this author a variety of symptoms, notably optic neuritis and a peculiar/

peculiar ataxic gait are observed in addition to a bilateral ophthalmoplegia, consciousness is markedly clouded, while death usually occurs in from ten to fifteen days, the illness throughout being unattended by any febrile disturbance. Superior polioencephalitis has been one of the rarities of clinical medicine, for the writer until recently cannot recall meeting with a case which resembled WERNICKE'S original description.

(6)

STRUMPELL in 1884 advocated the view that the cerebral palsies of childhood were dependent upon an encephalitis of the cerebral cortex, probably similar in its nature to the polio-myelitis of the spinal cord. Post-mortem evidence was, however, wanting in support of this hypothesis, for no cases had been examined in the early stage, while in chronic cases a porencephaly, extending sometimes to the lateral ventricles, was often met with, a lesion which was not to be accounted for by an inflammatory process limited to the grey matter of the cortex as STRUMPELL had presupposed. STRUMPELL, consequently, abandoned the term Polioencephalitis, which he had introduced to denote these cases and in his subsequent writings speaks of the Encephalitis of Childhood.

MEDIN/

(7)

MEDIN, a Swedish Physician who, at the Berlin meeting of the International Medical Congress in 1890, reported an outbreak of poliomyelitis in Stockholm, was the first to indicate that cerebral paralytic symptoms were far from uncommon in epidemic poliomyelitis, while the dependence of these symptoms upon an encephalitis has since been demonstrated by a number of observers. The question of a possible relationship between polioencephalitis, the encephalitis which is obviously due to the same virus as poliomyelitis, and encephalitis lethargica will be discussed in some detail later.

In the works of the earlier writers as in those of modern authors, the occasional occurrence of an encephalitis as a sequel to one of the infective fevers, is repeatedly referred to. OPPENHEIM⁽¹⁶⁾ in his monograph enumerates a long list of fevers and other infective disorders, in the course of which an encephalitis has been noted, e.g., influenza, scarlet fever, typhoid, pneumonia, erysipelas, whooping cough, mumps, diphtheria, measles, ulcerative endocarditis, suppurative otitis, ~~putrid~~ purulent bronchitis, etc. Although the occurrence of encephalitis as a sequel to these various infective fevers is an event of great rarity, as may be gathered from a perusal of the works of MURCHISON, GOODALL, CLAUDE KER/

KER and other authorities, it must be admitted that in very exceptional instances the virus of these various infective fevers may attack the nervous system, unless, and this is a possibility, the apparent association is to be explained by coincidence, or unless there has been an error in diagnosis, the febrile stage of the encephalitis having been mistaken for one of the exanthemata. Influenza is the one infective fever which demands special consideration in this connection. As will be indicated later, influenza has been very rife in the past year, during which period these cases of encephalitis have been observed. Further, so long ago as 1890,

(8)
LEICHTENSTERN drew attention to a possible relationship between the two affections, while several other German observers recorded isolated cases of encephalitis following influenza, during this, the first great epidemic of the latter disease to be observed in modern times. This subject will come up later for fuller consideration.

CLASSIFICATION of ENCEPHALITIS.

Excluding brain abscess and the secondary encephalitis which occurs in association with meningitis or in the neighbourhood ^{of} softenings and tumours, a tentative classification of what may be termed "Acute/

"Acute Primary Non-suppurative Encephalitis" might until recently, have been regarded as including the following recognised groups:-

1. (Encephalitis neonatorum, as described by VIRCHOW).
2. The Superior Polioencephalitis of WERNICKE.
3. The Encephalitis of Childhood differentiated in the first instance by STRUMPELL.
4. Polioencephalitis. In other words, the encephalitis which is met with in association with acute poliomyelitis as first demonstrated by MEDIN.
5. Encephalitis following a variety of acute infectious disorders.

All of these conditions, be it observed, are rare, as will be seen by anyone who cares to peruse the literature. Indeed, prior to the past twelve months, apart from a few cases of infantile cerebral palsy, and three or four instances in which cerebral paralyses occurred in association with poliomyelitis, the writer cannot recollect a single occasion in which he has made, or has seen others make a diagnosis of primary acute non-suppurative encephalitis.

ENCEPHALITIS LETHARGICA.

A new clinical picture has appeared within
(19)
the past year. VON ECONOMO appears to have been
the/

the first to report the presence of this new type of disease. This author described cases in Austria, in the autumn of 1917, apparently similar to those which are being met with in this country at the present time. NETTER of Paris, in the early months of 1918, drew the attention of the profession to cases of a similar kind occurring in the French capital. In April of last year, WILFRID HARRIS of St. Mary's Hospital, and ARTHUR HALL of Sheffield, contributed papers to "The Lancet", entitled respectively "Acute Infective Ophthalmoplegia" or Botulism" and "a note on an epidemic of Toxic Ophthalmoplegia". Since the appearance of these publications, numerous reports of isolated cases have appeared in the literature, and there have been two or three discussions upon the subject at Sectional Meetings of the Royal Society of Medicine. The attention of the Public Health authorities was speedily attracted by the title of HARRIS' paper, in which the suggestion was advanced that the condition was possibly "Botulism". The facts that the symptoms were similar to those met with in Botulism, that Botulism had been for long recognised in Germany, that this country was at War with Germany and that Botulism is due to a definite organism which is capable of cultivation, at once aroused public interest and apprehension, as may be seen/

seen by the numerous allusions to the subject in the public press, in the early summer of 1918. Was it possible that Botulism was being introduced intentionally into this country? Within three days of the publication of HARRIS and HALL'S papers, the Medical Research Committee took up the matter and made arrangement for a series of thorough bacteriological investigations, while the Local Government Board instituted an enquiry, the result of which was published in a Blue Book a month or two ago, under the title "Report of an Enquiry into an obscure disease - Encephalitis Lethargica". Although a number of isolated communications have been contributed to the Royal Society of Medicine, the Medical Societies of Paris, and to some of the medical journals in this country and in France, no attempt has been made, with the exception of the Blue Book above referred to, to deal with the subject in a systematic manner.

The writer's experience of Encephalitis Lethargica commenced in the Spring of last year. The first case in which he made a definite diagnosis occurred in April. Altogether the writer has now seen some thirty cases. On looking over the notes of nearly nine thousand cases, seen either in private or Hospital practice, he can only single out two or three/

three possible examples of the disease met with prior to this time. Further, the writer has observed within the past year, several anomalous cases in which the clinical facts indicated that an infective process of unknown nature had attacked the brain, spinal cord, or peripheral nerves respectively. Since it is just possible that the pathological virus may be the same as that which produces encephalitis, a note of several such cases has been included in this thesis.

N O M E N C L A T U R E .

Among a number of names applied to this disease are the following:-

	(19)
Encephalitis Lethargica (ECONOMO)	(23)
Encéphalite léthargique epidémique (NETTER)	
Acute Infective Ophthalmoplegia or Botulism	
	(25) HARRIS (24)
Toxic Ophthalmoplegia (HALL)	
Epidemic Polio-encephalitis (so called epidemic Botulism) (MELLAND) (38)	
Epidemic encephalitis (WILSON) (40)	
	(33)

BATTEN and STILL have applied the term Epidemic Stupor to a condition presenting somewhat similar features, which they have met with in infants.

Lethargic Encephalitis, by which title the new disease is coming to be generally known, would seem to be, in the present state of knowledge, an appropriate designation since this nomenclature indicates/

indicates both the nature of the pathological process, and at the same time, a very striking clinical feature of, at any rate, a certain group of cases. A word of caution is, however, in the writer's opinion, necessary in this connection, for, since lethargy is very possibly a focal mesencephalic symptom, further observations may demonstrate, as has just been indicated, that cases occur in which parts of the nervous system, other than the mesencephalon are affected, and that in these cases lethargy is not observed. Further pathological advances may, consequently, demand a change of nomenclature.

DESCRIPTION of a TYPICAL CASE.

A description of the clinical features presented by a typical case will serve as an introduction to a detailed account of the disease.

CASE I. Lance Corporal M.T., aged 21, attached to the Royal Engineers, was admitted to the Neurological Department of the 2nd Scottish General Hospital under the writer's care on the 10th of January, 1919.

The patient stated that he had been employed as a Clerk prior to enlisting in November 1916, and that his health had been very good apart from the fact that he had had an attack of dry pleurisy at the age of 15, and that he had been for some years troubled with occasional attacks of conjunctivitis, on account of which he had not been passed for service overseas. Venereal infection/

Name Land - Cpl. M. J.

Name Land - Cpl. M. J.



infection was denied. The patient had been a life-long total abstainer. There was nothing of note in the family history.

Upon 6th December 1918, some months previous to which time he had been living in rooms at Clerk Street, Edinburgh, the patient was admitted to the Ear and Throat Department of the Hospital suffering from nasal polyp~~is~~ which were occasioning nasal obstruction and much discharge from both nostrils. Soon after admission the polypi were ~~en~~snared. The day following the operation, he had an attack of conjunctivitis, This gradually cleared up, but he became morose, listless and drowsy, and complained of increasing difficulty in seeing. The eye examination failed to reveal anything abnormal. A right sided facial paresis was noticed. He complained of severe headache for several days, and became very drowsy, sleeping all day and night unless purposely roused, when he would answer quite intelligently. The temperature was slightly raised for a few days, reaching 100° on one occasion.

When examined upon January 10th, the patient was found to be well nourished and his muscularity was good. The temperature was 99.4 and the pulse 88. The physiognomy was very striking. The face was immobile and expressionless and there was a moderate degree of ptosis, rather more marked on the left side, the lids half covering the pupils. He was somewhat drowsy and his responses were slow, though to the point, his articulation being somewhat indistinct. The Ward sister stated that he sometimes muttered to himself, his conversation always referred to his military duties, while she stated that on the previous day, she had noticed him plucking at the bed-clothes. The optic axes were parallel. There was a marked paresis of the ocular movements. The upward movement of the eyes was good. The eyes could not be moved in a downward direction beyond the middle line. Movement of the right eye to the right was distinctly defective/

defective, while movements of both eyes to the left was slightly impaired. Vertical nystagmus was noted when the patient looked upwards, lateral nystagmus when he looked to either side. The pupils were rather large, the right being a shade larger than the left. Both reacted to light, but very poorly, while the reaction on attempted accommodation was also defective. The optic discs presented a healthy appearance. Distinct weakness of the right side of the face more particularly of its lower half, was present. There was no weakness of the jaw muscles, nor was there any difficulty in swallowing. The tongue was protruded straight but was somewhat dry and tremulous. There was no Kernig or neck rigidity. The knee-jerks were present, equal and not exaggerated; the plantar reflexes were of the flexor type, while the abdominal reflexes were equal and active. Pains at first sharp, latterly somewhat aching in character, were complained of in both arms, chiefly below the elbows. No objective sensory disturbance was detected, although when the drowsy state was most pronounced, there had been some incontinence of urine. This had only occurred on two or three occasions. Constipation had been, from the first, very marked. The other organs showed no signs of disease. A small quantity of mucopurulent sputum probably came from the naso-pharynx, for physical examination of the lungs revealed nothing abnormal. The heart was not enlarged and the sounds were closed. The radial arteries were not thickened, and the systolic pressure was 135. Neither the liver nor spleen were palpable. The urine contained neither albumen nor sugar.

Examination of the blood gave a red count of 4,800,000; the Haemoglobin was 80%; the leucocytes numbered 6,550, a differential count showed Polymorphs 68%; large lymphocytes 12%; small lymphocytes 19%; Basophiles 0.5; Myelocytes 0.5. The glycogen reaction was normal.

On lumbar puncture the fluid which was obtained was not under pressure and contained no excess of cells.

The/

The blood serum gave a negative result both to the Wassermann and Widal tests.

Examination of the sputum showed no tubercle bacilli, but enormous numbers of bacteria, especially cocci of different types some pneumococci, many strepto and staphylococci, also many short gram positive diphtheroid bacilli (Reference will be made to these organisms later).

No microorganisms were found either in the blood, urine or cerebrospinal fluid, nor was the *Bacillus Botulinus* found in the stools. d

The patient's condition remained practically stationary for several weeks, after which he began to slowly improve. A variety of drugs were used in his case, but of none could it be definitely said that they had an undoubtedly beneficial effect. By the end of March 1919, the patient was very much better in every way, although his physiognomy was still characteristic.

SALIENT CLINICAL FEATURES.

The symptoms which typically characterise Lethargic Encephalitis are, for the most part, illustrated in the history of the case above described. They may be conveniently classed in three groups, as follows:-

1. A state of Somnolence or Lethargy from which the affection derives its very appropriate designation. This symptom, which is present in the great majority of cases, is associated with/

with slow mental action, want of initiative and when pronounced, as a rule with an occupational delirium.

2. Febrile Disturbance which is met with almost invariably, in the earlier stages. Although, as a rule, slight in degree and consequently apt to escape detection, this symptom is very important in relation to diagnosis. Accompanying the fever certain general symptoms, such as headache and, it may be, giddiness and vomiting, are often met with during the earlier days of the illness.
3. Symptoms attributable to a local disorder of function of the brain stem, among which pareses of the ocular muscles, particularly those supplied by the third nerves, and of the face, are the most frequent.

PERSONAL EXPERIENCE
utilised for
PURPOSES of ANALYSIS.

The following account of the symptomatology and etiology of encephalitis lethargica, is based upon the records of twenty selected cases, in all of which the diagnosis was beyond question. During the months of February and March of the present year, the writer has met with nine additional cases, the records of some of which are reported later, though they have not been utilised in the subsequent analytical enquiry. These twenty-nine cases do not include an anomalous group, instances of which will be reported, in which there is evidence for believing that symptoms referable to the cerebrum, spinal cord and peripheral nerves, may very possibly have been produced by the same pathological virus.

ETIOLOGY.

An analysis of the series of cases above referred to permits of the following conclusions:-

SEX. The sexes were equally affected, ten patients being males, ten females. Of the female patients, five were married, five unmarried./

AGE. The average age was 38 years, that of the male cases being 39.2, that of the females 36.7. The oldest patient was aged 63, the youngest 18. In fifteen cases (75%) the age of onset was between 20 and 50.

OCCUPATION. There is nothing of special note in this connection. Four patients were soldiers who were admitted to the writer's wards in the 2nd SCOTTISH GENERAL HOSPITAL, three patients were business men, two were Arts students, while a lawyer, a ship's stoker, a motor-car driver and a tweed darning, were among those affected. Female patients were, for the most part, engaged in household work.

DOMICILE. Seven patients were attacked while living in Edinburgh or Leith. As will be seen from the accompanying plan, they were not living in any particular area of the town. One patient was an inmate of Craigleith Hospital at the time he was taken ill, the others were living in the following localities, viz:-

Bridge of Allan,
Kinross, ~~181, 182, 183, 184, 185, 186, 187, 188, 189, 190, 191, 192, 193, 194, 195, 196, 197, 198, 199, 200, 201, 202, 203, 204, 205, 206, 207, 208, 209, 210, 211, 212, 213, 214, 215, 216, 217, 218, 219, 220, 221, 222, 223, 224, 225, 226, 227, 228, 229, 230, 231, 232, 233, 234, 235, 236, 237, 238, 239, 240, 241, 242, 243, 244, 245, 246, 247, 248, 249, 250, 251, 252, 253, 254, 255, 256, 257, 258, 259, 260, 261, 262, 263, 264, 265, 266, 267, 268, 269, 270, 271, 272, 273, 274, 275, 276, 277, 278, 279, 280, 281, 282, 283, 284, 285, 286, 287, 288, 289, 290, 291, 292, 293, 294, 295, 296, 297, 298, 299, 300, 301, 302, 303, 304, 305, 306, 307, 308, 309, 310, 311, 312, 313, 314, 315, 316, 317, 318, 319, 320, 321, 322, 323, 324, 325, 326, 327, 328, 329, 330, 331, 332, 333, 334, 335, 336, 337, 338, 339, 340, 341, 342, 343, 344, 345, 346, 347, 348, 349, 350, 351, 352, 353, 354, 355, 356, 357, 358, 359, 360, 361, 362, 363, 364, 365, 366, 367, 368, 369, 370, 371, 372, 373, 374, 375, 376, 377, 378, 379, 380, 381, 382, 383, 384, 385, 386, 387, 388, 389, 390, 391, 392, 393, 394, 395, 396, 397, 398, 399, 400, 401, 402, 403, 404, 405, 406, 407, 408, 409, 410, 411, 412, 413, 414, 415, 416, 417, 418, 419, 420, 421, 422, 423, 424, 425, 426, 427, 428, 429, 430, 431, 432, 433, 434, 435, 436, 437, 438, 439, 440, 441, 442, 443, 444, 445, 446, 447, 448, 449, 450, 451, 452, 453, 454, 455, 456, 457, 458, 459, 460, 461, 462, 463, 464, 465, 466, 467, 468, 469, 470, 471, 472, 473, 474, 475, 476, 477, 478, 479, 480, 481, 482, 483, 484, 485, 486, 487, 488, 489, 490, 491, 492, 493, 494, 495, 496, 497, 498, 499, 500, 501, 502, 503, 504, 505, 506, 507, 508, 509, 510, 511, 512, 513, 514, 515, 516, 517, 518, 519, 520, 521, 522, 523, 524, 525, 526, 527, 528, 529, 530, 531, 532, 533, 534, 535, 536, 537, 538, 539, 540, 541, 542, 543, 544, 545, 546, 547, 548, 549, 550, 551, 552, 553, 554, 555, 556, 557, 558, 559, 560, 561, 562, 563, 564, 565, 566, 567, 568, 569, 570, 571, 572, 573, 574, 575, 576, 577, 578, 579, 580, 581, 582, 583, 584, 585, 586, 587, 588, 589, 590, 591, 592, 593, 594, 595, 596, 597, 598, 599, 600, 601, 602, 603, 604, 605, 606, 607, 608, 609, 610, 611, 612, 613, 614, 615, 616, 617, 618, 619, 620, 621, 622, 623, 624, 625, 626, 627, 628, 629, 630, 631, 632, 633, 634, 635, 636, 637, 638, 639, 640, 641, 642, 643, 644, 645, 646, 647, 648, 649, 650, 651, 652, 653, 654, 655, 656, 657, 658, 659, 660, 661, 662, 663, 664, 665, 666, 667, 668, 669, 670, 671, 672, 673, 674, 675, 676, 677, 678, 679, 680, 681, 682, 683, 684, 685, 686, 687, 688, 689, 690, 691, 692, 693, 694, 695, 696, 697, 698, 699, 700, 701, 702, 703, 704, 705, 706, 707, 708, 709, 710, 711, 712, 713, 714, 715, 716, 717, 718, 719, 720, 721, 722, 723, 724, 725, 726, 727, 728, 729, 730, 731, 732, 733, 734, 735, 736, 737, 738, 739, 740, 741, 742, 743, 744, 745, 746, 747, 748, 749, 750, 751, 752, 753, 754, 755, 756, 757, 758, 759, 760, 761, 762, 763, 764, 765, 766, 767, 768, 769, 770, 771, 772, 773, 774, 775, 776, 777, 778, 779, 780, 781, 782, 783, 784, 785, 786, 787, 788, 789, 790, 791, 792, 793, 794, 795, 796, 797, 798, 799, 800, 801, 802, 803, 804, 805, 806, 807, 808, 809, 810, 811, 812, 813, 814, 815, 816, 817, 818, 819, 820, 821, 822, 823, 824, 825, 826, 827, 828, 829, 830, 831, 832, 833, 834, 835, 836, 837, 838, 839, 840, 841, 842, 843, 844, 845, 846, 847, 848, 849, 850, 851, 852, 853, 854, 855, 856, 857, 858, 859, 860, 861, 862, 863, 864, 865, 866, 867, 868, 869, 870, 871, 872, 873, 874, 875, 876, 877, 878, 879, 880, 881, 882, 883, 884, 885, 886, 887, 888, 889, 890, 891, 892, 893, 894, 895, 896, 897, 898, 899, 900, 901, 902, 903, 904, 905, 906, 907, 908, 909, 910, 911, 912, 913, 914, 915, 916, 917, 918, 919, 920, 921, 922, 923, 924, 925, 926, 927, 928, 929, 930, 931, 932, 933, 934, 935, 936, 937, 938, 939, 940, 941, 942, 943, 944, 945, 946, 947, 948, 949, 950, 951, 952, 953, 954, 955, 956, 957, 958, 959, 960, 961, 962, 963, 964, 965, 966, 967, 968, 969, 970, 971, 972, 973, 974, 975, 976, 977, 978, 979, 980, 981, 982, 983, 984, 985, 986, 987, 988, 989, 990, 991, 992, 993, 994, 995, 996, 997, 998, 999, 1000~~
Dunfermline
Juniper Green/

Juniper Green,
 Methil (Fife)
 Hawick,
 Crieff,
 Kirkcaldy,
 Stobo (Peebles) and
 Carlisle.

One patient was attacked when on board H.M.S. Princess Royal at the time stationed at Rosyth. It is interesting to note that only one patient was living in an isolated country house, when her symptoms developed.

SOCIAL STANDING. The majority of the patients affected, lived in comfortable circumstances and belonged either to the middle or well-to-do lower classes.

SEASONAL INCIDENCE. This is a point of some interest. The month of onset in the twenty cases was as follows:-

March	1		
April	2		
May	1		
June	2	July	0
August	1	September	0
November	2	October	0
December	5		
January	3		
February	3		

Although it must be admitted that deductions based upon such a small number of cases are open to fallacy, the writer is of opinion, after a careful consideration of the facts and possible fallacies, that the/

the conclusion is justified, that cases of Encephalitis Letargica have been more frequent of late than during the Spring and Summer of 1918. Further, since only one case in the present series developed during the months of July, August, September and October, as compared with thirteen during the months of November, December, January and February, the suggestion is put forward, that the affection may be one which occurs more especially in the cold months of the year. (52)
Dr. S. P. JAMES, in analysing the material collected by the Local Government Board, says:-

"Most of the cases reported occurred during the seven weeks between the 16th of March and the 4th of May, and according to the figures the disease reached its maximum prevalence somewhat slowly, maintained this prevalence for a comparatively brief period and gradually declined".

He further adds:-

"We hazard the conjecture that for the country generally, the number of cases reported are less an index of the seasonal prevalence of a new disease than they are an index of the rise and decline of activity in discovering and reporting cases of an old one". "This conjecture", he goes on to state, "is supported by the fact that con-
temporary/

"contemporary and lay literature on the subject coincided with the chief incidence of cases, the "dates of onset, (but not the dates of notification) being equally distributed on each side of "the 20th April, the day on which attention was "first directed to the subject in the Medical "Press".

It is precisely on a point of this kind that the experience of an individual observer is of special value. After a scrutiny of the notes of all the cases he has seen, either in Consulting or Hospital practice during the past year, the writer is satisfied that Encephalitis Lethargica has been more prevalent in this part of the country during the past few months, and that the increased prevalence is not merely an apparent increase, accounted for on the assumption that cases had escaped recognition during the earlier part of the year. Further, in only three of the cases included in the present series, was the condition suspected by the medical man in charge, a fact which indicates that the attention of Practitioners throughout the country has not been, as yet, specially drawn to the disease and their interest in consequence aroused. Again the facts suggest that the disease is one which is apt to occur during the colder/

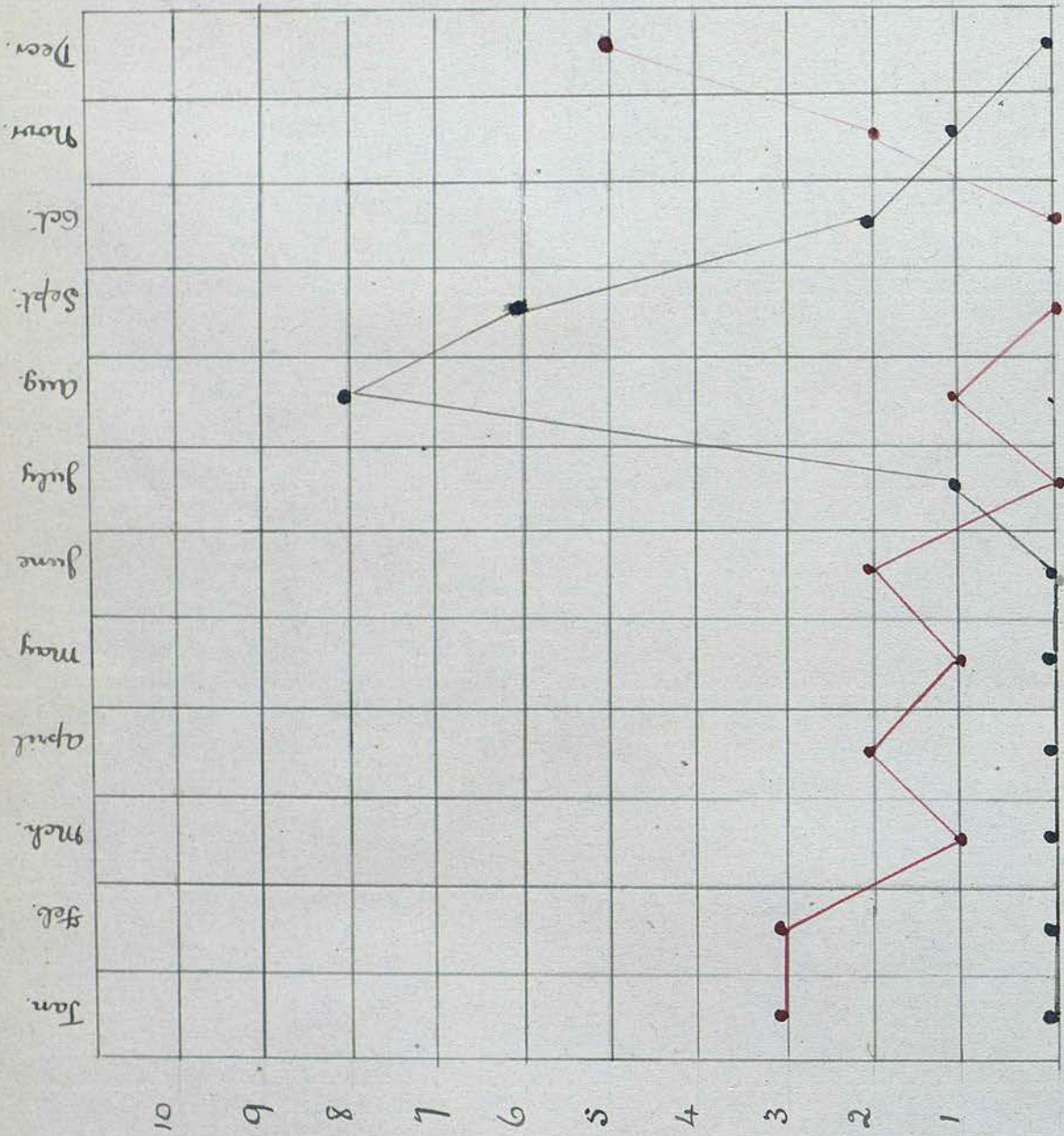


Chart comparing the seasonal incidence as regards date of onset in the twenty selected cases of encephalitis referred to in this thesis with that of 184 cases of acute poliomyelitis observed by the writer during the years 1910 to 1913.

colder rather than during the warmer months of the year.

This suggestion of a seasonal incidence is of interest, in relation to poliomyelitis, since the view has been advanced that Encephalitis Lethargica may be a modified form of this disease. In this connection a chart has been drawn up comparing the seasonal incidence, as regards the month of onset of the present series of cases, with that of eighteen cases of acute poliomyelitis seen by the writer during the years 1910, 1911, 1912, 1913. It is well to add, that the curve for the poliomyelitis cases conforms very closely with the acknowledged incidence of this disease. A study of the chart shows that the onset of 16 cases of Lethargic Encephalitis and ¹/~~3~~ cases of Poliomyelitis was, during the winter and spring months (November to April) while that of ¹⁷/~~15~~ cases of Poliomyelitis and only 4 cases of Lethargic Encephalitis was during the summer and autumn (May to October).

PREVIOUS HEALTH. There is nothing calling for special comment in this relation. The great majority of the patients were in good health at the time of onset. One patient had a healed tuberculous lung, another had suffered from what had probably been a tuberculous pleurisy, a third had pronounced aortic valvular/

valvular disease, while a fourth had, for some years been subject to occasional attacks of conjunctivitis. In no case was a history of Syphilis forthcoming, nor was there evidence of this disease in any single instance. The Wassermann reaction on the blood serum was negative in the five cases in which it was examined. The same applies to the cerebro-spinal fluid, which was examined in three cases. Alcohol appears to play no part in relation to this disease. In no case was there a history of alcoholic excess. Several of the patients had, indeed, been life-long abstainers.

PRECEDING ILLNESS. Two patients had suffered from a cold in the head for a week or two, prior to the onset of the Encephalitis, while another stated, that he had given his head a rather severe blow, in consequence of which he had felt somewhat dazed for a few minutes, two or three days before the first symptoms appeared. A mental shock preceded the onset by a few days in one case. One patient had been treated for boils over the sacrum for some weeks prior to her illness. The case which has been already reported as a typical example of the disease is of some interest, for this patient had suffered from conjunctivitis at times for several years, while/

while his symptoms developed in Hospital, immediately after an operation for the removal of a nasal polypus, which had been causing a profuse nasal discharge.

The frequency of influenza during the past year, led the writer to make a special enquiry as to preceding attacks of this affection. Although he had expected to very probably find an association between the two conditions, this was not so, for in only three instances was there a history of an attack of influenza during the few weeks which immediately preceded the onset of the Encephalitis, and in not one of these was there certain proof that the diagnosis of influenza had been correct. It is indeed, quite possible, that in more than one of these cases, as in several which have not been included in the present series, the onset of the febrile stage of the Encephalitis had been erroneously regarded as the consequence of an influenzal infection.

INFECTION by CONTAGION.

In no instance which has come under the writer's personal notice, have two members of a family or of a household been affected, nor has he met with a single case in which the disease might be regarded as having been acquired by a healthy person coming/

coming in contact with a case of encephalitis, or in which a healthy person was suspected of being a carrier of infection. HARRIS, however, reports the case of a patient who was taken ill with encephalitis on March 29th and gave birth to a child on April 7th. The child was cyanosed at birth, and a few days later suffered from marked drowsiness, constipation and retention of urine. Both mother and child eventually recovered. MACNALT, too, refers to the case of a woman suffering from encephalitis, who gave birth to a child which subsequently exhibited mild symptoms of the disease, two other children in the family being at the same time similarly affected.

MODE of ONSET.

The onset of encephalitis lethargica is not uncommonly preceded by a prodromal stage characterised by premonitory symptoms. In some cases the symptoms develop gradually. Sometimes the patient goes to bed feeling in his usual health, to awake in the morning with the first indications of the disease, while exceptionally the onset is apoplecticiform in its suddenness and severity.

The/

The premonitory symptoms which may be observed are various. Thus, several patients complained of defective vision for some days before the development of any further manifestations. One patient, who complained of this symptom when first examined, presented no objective signs with the exception of a very marked nystagmus. Subsequently, she developed pronounced symptoms. Pains in the limbs were very conspicuous features in the early stages of two cases, in one of which a sciatica, in the other a brachial neuritis was diagnosed. Again, it would seem from a scrutiny of the history in some cases, that a febrile attack, without focal brain symptoms, and often erroneously attributed to influenza, may precede other definite indications of encephalitis by a week or two, the patient returning to his occupation during the intervening period. It sometimes happens, that even after the appearance of such symptoms as diplopia, giddiness or a degree of drowsiness, the patient is able to continue his work for a few days. In several cases the patient went to bed feeling quite well and awakened next morning complaining of light-headedness, giddiness, or diplopia. Again, the symptoms may come on with the rapidity of a cerebral haemorrhage, as/

as in the case of a female patient who suddenly fell down in a comatose state.

An accurate estimate as to the frequency of the individual symptoms first noticed, is not possible in the present series, for, as already mentioned, the majority of the cases were seen on only one or, it may be, two occasions, while some of the patients when seen, were so drowsy and their responses so slow, that it was difficult to elicit a satisfactory history. Other patients were not seen until some weeks after the onset of the illness and, as is well-known, the memory in illness is often defective as regards details, which to the physician may be of both interest and importance. Further, the minds of some patients affected with encephalitis lethargica may be a blank as regards the earlier part of their illness. Lastly, the notes dictated often from memory, some hours after the case was seen, are not always as complete as might be wished. Suffice it to say, that diplopia was noted as the first symptom in ten cases, headache in 7 cases, giddiness in 5 cases, defective vision in 4 cases, and vomiting in 2 cases, while drowsiness, slight febrile disturbance, a dry tongue and pronounced constipation were all symptoms which were repeatedly referred to, as amongst the earliest manifestations noted by the patient.

SYMPTOMATOLOGY/

SYMPTOMATOLOGY.

The salient clinical features have been referred to and exemplified in the report of a typical case. The individual symptoms will now be considered in detail.

THE LETHARGIC STATE.

Lethargy, Somnolence or Stupor was noted in 18 Cases, (90%) of the present series.

The lethargic state constituted the most striking feature in many of the cases and was commonly one of the earliest manifestations, developing with the suddenness of an apoplexy in one instance, with comparative suddenness in others. The on-set in the great majority was more gradual.

The degree of lethargy varies greatly in different cases, from slight drowsiness with a constant inclination to go to sleep, to a state of actual coma. Thus, one patient dropped off to sleep, while sitting in a chair as the writer was taking notes of his case. The wife of one patient said:- "He would be talking to you and would be asleep directly". The sister of another patient said: "She was so drowsy we had to shake her to waken her in the morning and to feed her. She went off into
"a/

"a sleep whenever we left her alone". Of another patient, the relatives, speaking of the early stages of his illness, said:- "He was sleeping all "the time". One patient remarked that his eyelids felt heavy and that he had difficulty in keeping his eyes open and in keeping awake. There was only a very slight degree of ptosis in this case. Sometimes it is possible for the patient to continue his work for several days after the state of drowsiness is first noticed. Again in some cases, the stupor is so pronounced as to amount to a state of coma, from which the patient cannot be roused. The degree of lethargy may vary from day to day, though not to any great extent, in individual cases. Unlike the drowsiness occasionally observed in other febrile conditions, this symptom may persist long after the temperature has fallen to the normal. Although the lethargy may continue for many weeks, it eventually passes off gradually and completely in those cases which recover.

Two patients presented no history of lethargy or drowsiness, and in several additional cases, the previous existence of these symptoms was only established in response to direct leading questions. This is a fact which is in the opinion of the writer of/

of considerable importance, since, as will be indicated in relation to the diagnosis, these cases are apt to escape recognition.

A restless, excitable condition sometimes replaces or alternates with the lethargic state in the early stages of the illness and in more than one case insomnia was, at times, a troublesome symptom.

MENTAL STATE. This is conveniently considered in relation to the lethargy and somnolence.

Prolongation of the reaction time is a term which aptly expresses the leading feature of the mental state in this disorder. Although the patient may be very drowsy and almost stuporose, yet when awakened, he usually replies intelligently to questions put to him. His responses, however, are slow, and it may be necessary to repeat a question several times, although when the answer does come, it is generally to the point, and evinces little or no indication of mental impairment.

Lack of mental initiative is another feature, which is very characteristic. When spoken to, the patient answers intelligently, yet he seldom makes a spontaneous remark, and he often lies for hours, making no attempt at voluntary movement, although he may be able to move his limbs quite satisfactorily, if asked to do so.

Delirium/

Delirium is observed in a considerable number of cases. Its presence was noted in eight (40%) of the present series. The type of delirium is of interest. In every case, it referred to the patient's occupation or recent actions. Thus one man was carrying on a conversation at an imaginary telephone. When addressed, he answered quite rationally, but a few minutes later he had returned to his telephone. A Sergeant was constantly engaged in giving orders to his men. Another patient was in the early stages of his illness, constantly occupied in dictating instructions to his clerks. A young girl imagined she was at a Dancing Class, while another patient's delirium had reference to an after-dinner speech he had delivered, the day before he was taken ill. Two or three patients had, for a time, to be constantly watched, since they made repeated attempts to get out of bed, purposing evidently, to return to work.

A highly emotional state is, it is affirmed by Dr. MACNALT⁽⁵²⁾, often observed in these cases - "the patient being described as 'strange in manner' and laughing and weeping without apparent cause". One patient seen by the writer in the early days of her illness "giggled and wept alternately, whenever any attempt was made to examine her", so wrote the House/

House Physician from the Hospital to which she was subsequently admitted. Another patient, seen on one occasion, appeared at the time of examination, to have lost her sense of orientation. Although she was in her own room, she did not appear to know where she was, - she looked about her in a startled way, - she failed at first, to recognise her father, and she mistook the identity of one or two of her relatives. These are the only two cases of the present series in which symptoms of a like nature were noted. The writer's experience would, consequently, not lead him to regard emotional instability as a characteristic or frequent feature of the clinical picture.

The memory for recent events, as compared ^{that for} with events which have happened in the distant past, is undoubtedly impaired, and when the lethargic state has been pronounced, these patients will often say on recovery, that they remember little or nothing of the early days of their illness.

TEMPERATURE. Some febrile disturbance is the rule in this affection. This was noted by the writer in all the cases seen by him within the first few days of the illness, while further enquiry elicited the fact, that in fifteen cases (75%) some elevation of temperature had been observed. Since the fever is usually slight and of short duration, it is probable/

probable that had special attention been directed to the point, the presence of pyrexia would have been recorded in a considerably larger percentage of cases if not in all.

The temperature usually rises with the appearance of the first symptoms, but in exceptional cases, no elevation was noted until a few days later. The degree of febrile disturbance is usually slight. In only three of the writer's cases did the temperature reach 102° and this on isolated occasions. An elevation of 104.6 was attained in one fatal case immediately prior to the patient's death, which was directly due to a bronchopneumonia. According to the Local Government Board enquiry "the common variation in temperature is between 101° and 102° F. while in some cases it swings to 103° or 104°".

The duration of the febrile disturbance varies. The conclusion come to by the Local Government Board enquiry, is that "the pyrexia usually lasts for two to five days but may continue for ten or even fourteen days, the fall to normal being sudden or gradual with oscillations". The appended charts which register the temperature records in the only three cases which were under the writer's direct observation for several weeks from the early stages of the illness, demonstrate that the febrile disturbance/

disturbance may, at any rate in certain cases, be of longer duration than this statement would indicate. Details of the three cases above referred to are as follows:-

SERGEANT D. Onset December 11th, 1918. Admitted to Hospital December 15th, 1918. The temperature curve up to January 7th, shewed a slight swing from 97° to 100°, the latter point being only reached on one or two occasions. From this date onwards, the temperature was consistently subnormal. (*vide p.p. 60 and 61*)

LANCE CORPORAL T. admitted to Hospital January 6th, 1918. a week or two after the onset of his illness. The temperature curve showed some slight elevation, reaching a maximum of 100, during the first four days after admission, but thereafter was constantly subnormal. (*vide p. 20*)

PTE. S. Onset of illness February 3rd, 1919.

Admitted to Hospital 16th February. The temperature was slightly raised (maximum 99.6) from the day of admission until February 22nd, but was constantly subnormal after this date. (*vide p. 86*)

Sometimes an isolated evening rise of temperature up to 99° or thereabouts may occur a considerable time after the actual febrile stage of the illness/

illness has passed off. This is an observation which may prove of value in diagnosis. Charts are appended indicating the course of the temperature in the cases above referred to.

THE PULSE. An increase in the pulse rate out of proportion to the pyrexia was noticed by the writer, in two or three cases, while in other patients in whom the temperature at the time was normal, a pulse rate of 85° to 100° was repeatedly recorded. This observation, if corroborated, may also prove to be a point of some diagnostic value. Apart from the increased rate, the condition of the pulse calls otherwise for no special comment.

The systolic blood pressure estimated by the Tyco's instrument in four cases, three of which were still in the febrile stage, was 135, 145, 115, and 144.

HEADACHE. Headache was complained of by 14 patients (70%). This symptom is, as a rule, present only during the early days of the illness. It is seldom severe, and since only a minority of the cases were seen during the febrile stage, information as to its character and site, is, in the present series, necessarily somewhat unsatisfactory. Two patients complained of unilateral temporal headache, one/

one suffered from a bilateral frontal headache which persisted for a fortnight, while a third patient ~~also~~ stated, that his headache had been located in the back of the head and neck. Severe neuralgic pain above the right eye was the earliest symptom in one case. In only one other case was the headache described as distressing. It is interesting to note that according to the Local Government Board enquiry, headache was also present in 70% of the collected cases, the headache being described as "commonly frontal, occasionally occipital, sometimes in both regions".

VERTIGO. The presence of this symptom was noted in seven cases(35%). One patient complained of intense giddiness whenever she attempted to lift her head off the pillow. Although in two cases, giddiness and diplopia were concomitant symptoms, the vertigo does not appear to have been of ocular origin, for it was not alleviated when the eyes were closed. In no case has the writer noticed the presence of tinnitus, which was met with in association with vertigo in three of the cases referred to in the Local Government Board enquiry. Admitting that this symptom was not specially enquired for, its presence would certainly have been recorded had the patient/

patient complained of it. Vertigo, when present, was in the majority of cases, a transient symptom, confined to the early days of the illness, although in two or three instances, it persisted during convalescence.

VOMITING. Vomiting occurred in five cases. (25%). It is a symptom which is sometimes met with in the first two or three days of the illness and is not observed in the later stages.

SPEECH, ~~/~~PHONATION and ARTICULATION. Aphasic defects or disturbances of speech proper were not met with in any of the writer's cases, although as already mentioned, the patient is often very slow in grasping the import of a question, while his responses are correspondingly tardy. He speaks slowly and in a monotonous way, preferring to confine his replies to monosyllables and seldom giving vent to a spontaneous remark. The absence of emotional expression and gesticulation, when the patient speaks is sometimes a very striking feature.

APHONIA was observed in one patient who was at the time in a stuporose state.

Defects of articulation noted in nine patients (45%) are constant in pronounced cases. The disturbance consists, as a rule, in some slight want of precision in pronunciation, and it may be some thickness or indistinctness of speech, while in/

in extreme cases articulations may be mumbling and almost or quite unintelligible. A definite nasal intonation was not observed in any of the cases seen by the writer.

SPECIAL SENSES. Vision shewed some disturbance in 15 cases (75%) of the present series.

Defective visual acuity, as has been mentioned, may be the earliest symptom of which the patient complains. Among 8 cases in which visual impairment was demonstrated or complained of, one patient remarked that he had been "bleary-eyed" since the onset of his trouble. Another patient stated, that when he tried to read, the letters ran into each other, while a third patient said, that objects appeared to be constantly moving. Visual defects would appear to be explained in most instances by paresis of accommodation, in some by nystagmus, in others by definite paresis of an ocular muscle. Photophobia was only complained of by one patient.

DIPLOPIA. This symptom was complained of by 12 patients (60%). It was noticed, almost without exception, as one of the earliest manifestations. The diplopia, in several instances was transient, passing off in the course of a few days, though in others it was persistent. Sometimes diplopia/

diplopia was accompanied by an obvious defect in the ocular movements, but this was by no means always the case. The writer is unable from his experience to express an opinion as to whether diplopia ever remains as a permanent symptom.

Contraction of the fields of vision, apart from that which might be accounted for by the ptosis present in some of the cases examined in this connection, was not observed in a single instance.

The optic discs examined in 15 cases, presented in each instance a healthy appearance, with the exception of one case in which some engorgement of the retinal veins was observed.

HEARING, TASTE, and SMELL. In no case was any defect of hearing noted. This remark applies also to the sense of taste and smell.

CRANIAL NERVES. Ocular Palsies constitute the most frequent focal symptoms in this disease. When paresis of the external muscles of the eye, ptosis, nystagmus, and pupillary abnormalities are included, evidence of defective action of the ocular muscles was indeed, noted in all but two cases in the present series (90%). The third nerve is especially involved and the paresis is often transient. When the Ophthalmoplegia is pronounced, it is usually bilateral and asymmetrical. The writer has met with no case in which a marked unilateral third nerve/

nerve palsy existed. In one patient the character of the diplopia pointed to the existence of paresis of the fourth nerve, while in two there was a tendency for both eyes to swing back towards the middle line, when an attempt was being made to maintain them in the position of extreme lateral deviation. The upward and downward movements of the eyes were impaired in several cases the defect being as a rule asymmetrical.

PTOSIS was noted in eight cases (40%). This varies from a very slight drooping of one or both lids to a ptosis so pronounced that the eyeballs are almost covered. It is interesting to note, that in two cases a slight degree of ptosis unilateral or bilateral was said to be natural to the patient. The ptosis is usually unaccompanied by frontal overaction, a circumstance which is either to be explained by an associated paresis of the facial muscles which was present in some cases, or, it may be, by the general state of mental lethargy.

NYSTAGMUS. The presence of nystagmus or nystagmoid movements was noted in 12 Cases (60%); in eight of these, the nystagmus was very marked, while in the four remaining, very definite movements, referred to as nystagmoid, since they were not sustained, were observed. As already indicated, the/

the nystagmus may be the only focal sign, while further it may cause some disturbance of vision. In no case was nystagmus observed when the eyes were in the position of rest. As a rule, the movements were only elicited on lateral deviation of the eyes, their direction being horizontal. The nystagmus may be more pronounced on looking to one side than to the other, or more marked in one eye than in its fellow. Exceptionally nystagmus was observed when the eyes were directed upwards, the movements then being vertical in direction. In one case nystagmus was only present when the patient looked upwards, while nystagmoid movements more pronounced on looking downwards than in other directions, were once recorded. Rotatory movements were noted in one case. The amplitude and rapidity of the movements vary greatly.

PUPILS. Some pupillary abnormality was recorded in eleven cases observed by the writer (55%). Inequality was noted on seven occasions. The size of the pupils does not, as a rule, call for comment, although in three cases there was a pronounced bilateral mydriasis. In no instance was a myosis observed.

A sluggish response to light was found in nine cases (45%) sometimes confined to one eye or noticeably/

ENCEPHALITIS LETHARGICA.



The Physiognomy in a typical case (Lance-Corporal M.T., page 21.).

noticeably more marked in one than in the other.

In only one case in which there was also a pronounced mydriasis, was the light reaction actually abolished, and this phenomenon, which was repeatedly confirmed, was merely transient. On several occasions the contraction of the pupils on convergence was noted to be defective or absent.

FACE. Paresis of the face ranks next in frequency to the ocular palsies among the focal symptoms met with, in this disease. Thus twelve of the writer's patients (60%) presented some abnormality of the facial musculature. In ten cases, weakness of the facial movements, five times unilateral, five times bilateral and varying in degree from a slight paralysis, to a complete facial paralysis was detected. The facial palsy was complete in two of the unilateral cases. In one of these, in which the paralysis of the face developed seven days after diplopia, (the first indication of disease,) was complained of, the Faradic excitability of the affected muscles was completely abolished, while the galvanic response was quite brisk. The paralysis in both these cases passed off completely within ten weeks.

A want of mobility of the face, very similar to the mask-like face of paralysis agitans, was noted/

noted on seven occasions. In two of these cases no definite weakness of the facial muscles was detected on further examination.

Tremulousness or unsteadiness of the facial musculature while the patient spoke, was observed in three cases.

DYSPHAGIA or difficulty in swallowing was a troublesome symptom in four patients in all of whom the lethargic state was, at the time, very pronounced.

PALATAL weakness was not recorded in a single instance.

The tongue was in the early stages of the illness almost invariably very dry and heavily coated and it was often tremulous. Excessive salivation was noted in one case.

MOTOR DISTURBANCES. Loss of power amounting to actual paralysis of the limbs was met with in no case, although in one there was a slight left-sided hemiparesis. Generalised muscular weakness or asthenia is, however, the rule in all but slight cases. The asthenia appears to vary to some extent with the degree of lethargy.

The patient, as already mentioned, may lie like a log for hours at a time, making no attempt to turn in bed or move his limbs. General muscular/

muscular feebleness may persist for months after the other symptoms have passed off.

Extreme extensor rigidity of the lower limbs with pointing of the toes was exhibited by two patients, while a slight degree of spasticity was observed in two other cases.

KERNIG'S sign was only twice met with, and in neither case was it pronounced, while rigidity of the neck, which was also slight in degree, was met with, on one occasion only. The absence of these signs in encephalitis, is a point of value in differentiating the disease from meningitis.

Tremor of a general character affecting the upper limbs, somewhat coarse in type and aggravated by volitional effort, was observed in at least six cases, in several of which there was also a tremor of the tongue and face. One patient presented a definite unilateral intention tremor, while in another a rhythmical pronation and supination tremor, identical with that met with in paralysis agitans, was confined to one arm and hand.

Plucking at the bed clothes was observed in five cases, all these patients at the time being in a state of profound lethargy.

CATATONIA was a striking symptom in several/

several cases, at a time when the lethargic state was at its height.

SENSATION. Sensory disturbances were seldom complained of. Two patients referred to pains in the limbs. In one of these cases the pains were severe and persisted for weeks after the lethargy, asthenia, and facial paralysis which were also present, had passed off.

In no case was the writer able to satisfy himself with certainty, as to the existence of any objective alteration in sensation, although it must be admitted that little time was devoted to the sensory examination which on account of the patient's mental state, was often unsatisfactory.

REFLEXES. The tendon reflexes (knee and ankle jerks) showed as a rule, no definite abnormality. Among seventeen cases in which the condition of the tendon jerks was noted, they were recorded as being normal in nine, exaggerated in two, diminished in four, very sluggish in one, but absent in none. In one case, a bilateral ankle clonus was obtained.

The plantar reflex in seventeen cases was found to be of the normal flexor type in twelve, definitely extensor in three, in one of which the extensor response was unilateral, and of an indefinite type in two cases.

The/

The abdominal reflexes, the condition of which was specially noted in seven cases, were found to be absent on both sides in three, present and fairly active in the remaining cases.

SPHINCTERS. Constipation often extreme in degree is the rule. It is reported as having been present in nine cases of the present series (45%). The proportion of cases in which this symptom occurred, is indeed, probably, considerably higher than these figures represent.

Retention of Urine was an early symptom in two cases, in each of which catheterisation was called for. One patient was actually recommended for admission to the Surgical side of a Hospital, on account of this symptom which was erroneously believed to be of the obstructive variety. Some difficulty in passing water was noted in several other cases.

Incontinence both of urine and faeces is, as might be expected, in view of the mental condition, a not uncommon incident, when the lethargy is profound.

SKIN ERUPTIONS. The presence of skin eruptions was remarked on, in quite a number of the cases collected by the Local Government Board. In only one of the writer's cases was the presence of a skin/

skin rash noted. The rash was of the scarlatinal type, and there was reason for believing that it may have been produced by enema. |an

Sweating is sometimes a prominent feature in the early days of the illness. In two cases very profuse unilateral hyperidrosis was noted.

URINE. The urine in one case contained a trace of albumen, while that of another patient, when admitted to Hospital, contained, it was affirmed, both sugar and acetone, on the first occasion upon which it was tested. Repeated examinations within the next few days, however, failed to discover any abnormality.

BLOOD. An examination of the blood was carried out in four cases.

	Sgt.D.	L.Cpl.T.	Pte.S.	Mr.B.
DATE of EXAMINATION	21.12.18	14.2.19.	26.2.19.	3. 1.19
TERMINATION of febrile stage	13.1.19	9.1.18.	23.2.19.	
RED BLOOD CELLS.		4,800000	5,700000	
HAEMOGLOBIN		80%	95%	
WHITE BLOOD CELLS	11,100	6,500	7,800	5,500
DIFFEREN- TIAL COUNT:-				
Polymorphs	68%	68%	62.6%	67.5%
Lymphocytes	22%	19%	26.3%	26.5%
Large mono- nuclears	8%	12%	8.6%	5.9%
Eosinophiles	2%	-	2%	.9%
Basophiles	-	.5%	.3%	
Myelocytes		.5%		
Glycogen Reaction		normal.		

The blood was examined in only one case (Sergt.D.) during the febrile stage, when a slight leucocytosis was found (vide supra). Otherwise the examination of the blood yielded nothing abnormal. A Bacteriological/

Bacteriological examination was carried out in two cases (in each instance) with a negative result. According to the Local Government Board enquiry "a clinical examination of the blood" was carried out in ten cases. The blood counts "were normal and cultures made from the blood remained sterile". (52)

CEREBRO—SPINAL FLUID. In seven cases, the cerebro-spinal fluid was examined. The fluid was in every case quite clear and was evidently not under pressure. One or two cases presented a slight increase of lymphocytes when examined by the rough method. No excess of albumen was observed.

The WASSERMANN REACTION tested on the blood serum in five patients, including three soldiers, was in each instance negative.

The WIDAL REACTION examined in three cases, was in two of these, found to be negative. In the third case, that of a civilian, the serum gave a positive reaction both to typhoid and paratyphoid B.

BACTERIOLOGICAL INVESTIGATIONS. The Bacteriology of the pharynx, sputum when present, blood, cerebro-spinal fluid, urine, and faeces was made/

made the subject of a special investigation in
several ^{cases}, by Dr. JAMES MILLER. The results of these
observations are included in this thesis. (p. 108)

CLINICAL TYPES and CASE RECORDS.

The diversity of the clinical features is a striking characteristic of this disease. A variety of types may be differentiated in accordance with either the predominance of the general or focal symptoms or with the character of the focal manifestations. The recognition of such types is useful as an aid in connection with the many problems in differential diagnosis which the malady presents, ~~characterised~~ ^S ~~ed by the symptomatic triad, viz:-~~

characterised by the ~~sympt~~ following symptoms viz:-
 TYPE I. The lethargic state, pyrexia and Focal nervous symptoms, referable notably to the mesencephalon.

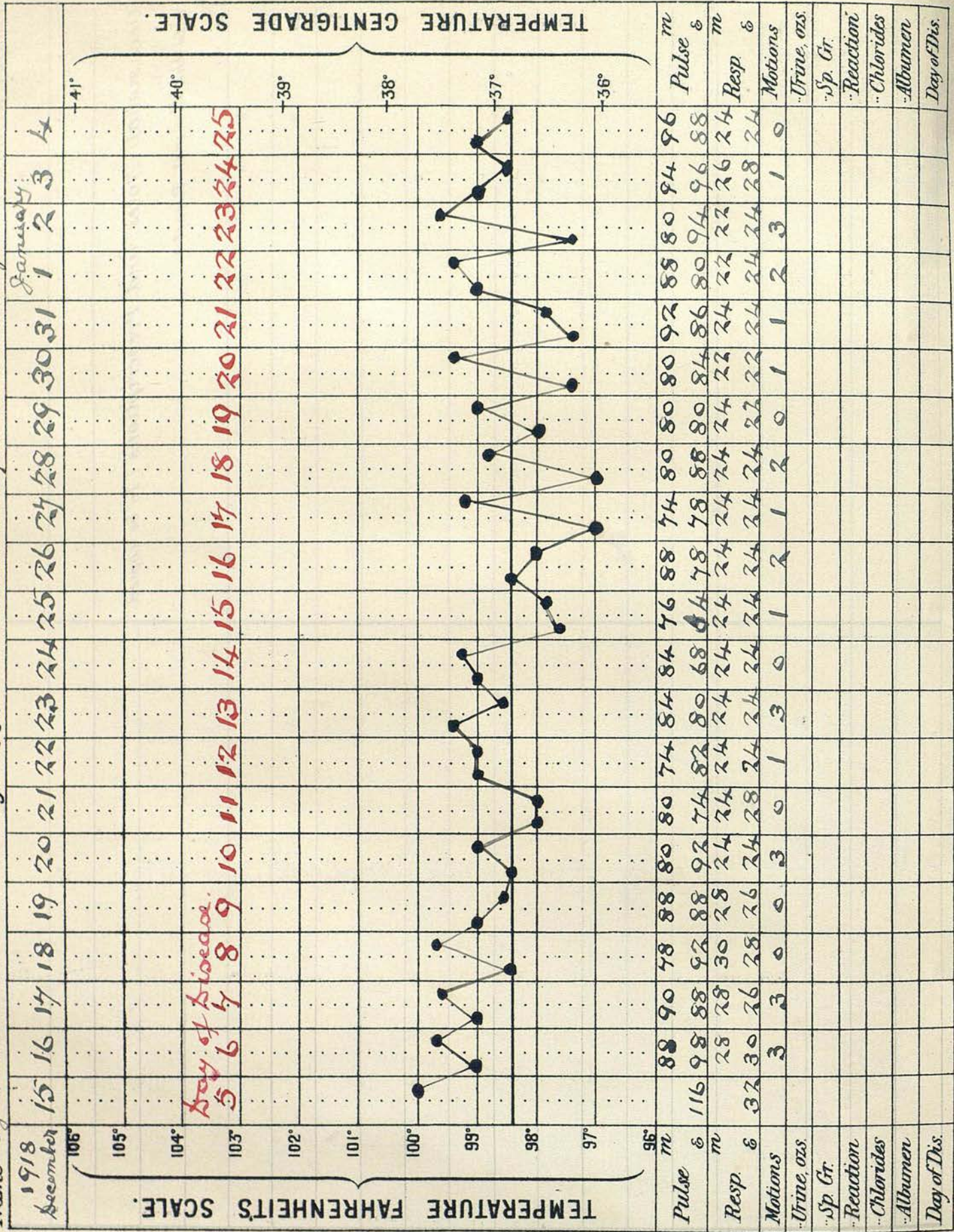
A typical severe case of Encephalitis Lethargica, such as that of Lance Corporal M.T., presents a very striking appearance. (See p. ⁴19). The patient usually lies on his back, the eyes closed or half-closed, the face it may be flushed and covered with beads of perspiration. He mutters to himself more or less incoherently, evidently imagining that he is engaged at his daily occupation. The lips are seen to move and yet the face may be quite expressionless, although perhaps somewhat tremulous. Every now and then the patient may be seen to fumble with his hands, as/

if arranging the bedclothes, and a pronounced tremor of the hands may be observed at these times. The physiognomy may, indeed recall that presented by a case of acute alcoholism. Even when the patient is in this semi-stuporose state, he will often pull himself together when spoken to and may reply quite intelligently, in answer to questions, although his responses are slow, his intonation monotonous, and his articulation indistinct. On further examination, one may find in addition to the ptosis and the immobility of the face, a slight divergent strabismus and some defect of the ocular movements, notably of the muscles supplied by the third nerves, nystagmus and it may be, unequal pupils which respond sluggishly to light. The movements of the limbs show, as a rule, no pronounced paresis, although there may be a considerable degree of general asthenia. The knee-jerks are commonly unaltered and the plantar response is usually of the flexor type. The temperature may be slightly raised and the pulse rate somewhat rapid, while the tongue is often dry and tremulous and the bowels constipated. There is seldom any rigidity of the neck, & Kernig's sign is not usually present. The fundus oculi presents a healthy appearance/

(Case II., p. 60.)

continued, p. 61

Name Sgt. D. Age 28. Disease Encephalitis Lethargica Result



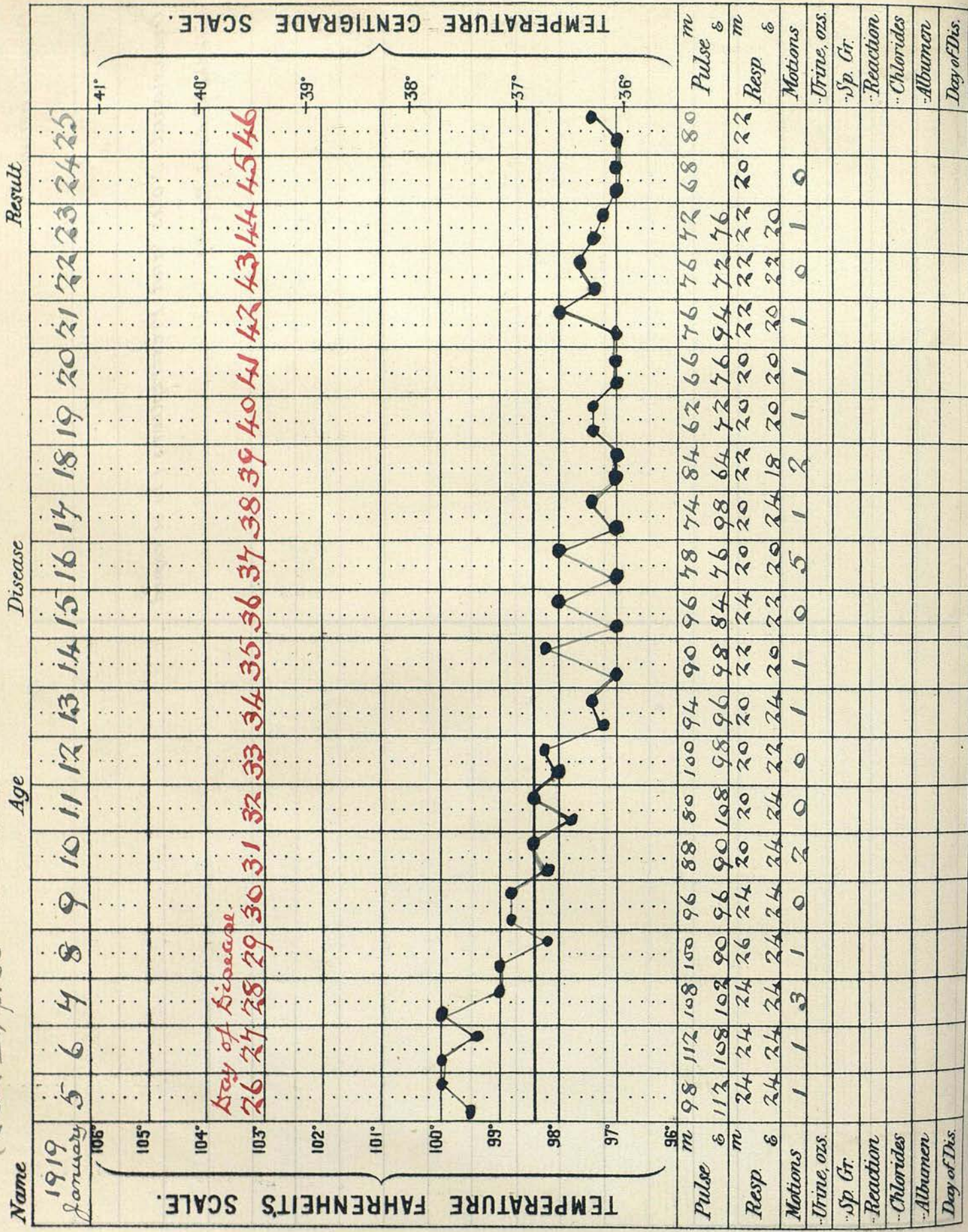
appearance. The blood shows little, if any increase of leucocytes and the fluid obtained on lumbar puncture, emerges in drops, and is quite clear, although it may contain a slight excess of cellular elements.

CASE II.

SERGEANT D., R.F.A., Aged 28. Admitted to the Neurological Department of the 2nd SCOTTISH GENERAL HOSPITAL on December 15th, 1918.

The patient was admitted to Flora Stevenson's School with influenza while on leave from France, in November 1918. There are no notes of his condition at that time, but from his statements, he would appear to have had a typical attack. Upon December 9th, he was sent to a Convalescent Hospital at Hawick, and on December 11th he stated that he was taken ill with a slight temperature and slight bitemporal headache. Upon the following day he saw double. According to the Medical Officer's report, the pupils were normal but sluggish to light. Kernig's and Babinski's signs were negative. The temperature was about 100°, the pulse rather fast, but the inspirations not increased. Nothing further was made out. Upon December 13th, he was stated to have been rather drowsy and there was a slight strabismus. The knee jerks were slightly increased. There was a slight cough, but nothing in the chest. Cerebrospinal meningitis was suspected and upon December 14th a lumbar puncture was made by Capt. Millar and some clear fluid withdrawn which was not under pressure. He was then transferred to Edinburgh.

When examined upon December 15th, the bladder was found to be distended and the urine was drawn off, - it contained no albumen. He was rather drowsy, and though quite intelligent and rational his attention was apt to wander after talking for a short time. The temperature was ~~98.8°~~^{100°}, the pulse ~~106°~~¹⁰⁶ and regular, the respirations ~~22~~³⁰, and the systolic blood pressure 135. The physiognomy/



physiognomy was striking. There was pronounced bilateral, symmetrical ptosis, the pupils being almost covered. The pupils were rather large, equal in size, and reacted sluggishly to light. The optic axes were parallel. Upward movement of the eyes was somewhat defective, especially on the left side. Diplopia was complained of immediately an attempt was made to raise the eyes above the horizontal. Downward movement of the eyes was slightly impaired; movement to the right was good but that to the left defective, notably the movement of the right eye. Nystagmus was present on lateral deviation, especially on looking to the left, the movements being rapid and of small amplitude. The fundus oculi was healthy. There was a bilateral paresis of the face. The movements of the jaws were satisfactory and there was no difficulty in swallowing. The tongue was protruded straight. It was very dry, and the patient stated that dryness of the mouth had been present for several days. Articulation was in no way abnormal, the patient understood everything said to him, and responded to questions intelligently, expressing himself clearly. Hearing was acute and there was no history of ear discharge. The hands were tremulous. There was considerable generalised weakness of the limbs, but no definite paresis, ataxia, sensory loss, astereognosis or muscular tenderness. The arm jerks were somewhat exaggerated & equal & the plantar response was flexion. The bowels had been constipated for some days and there had been some difficulty in passing water. There had been no vomiting. The abdomen was somewhat distended and tympanitic; the liver was not enlarged; the spleen was not palpable; and there was no rash. The heart sounds were pure and the organ was not enlarged.

The same evening it is noted that the patient was "inclined to wander", issuing orders to his men, while he plucked at the bedclothes with his fingers. He was intensely drowsy. There was quite a marked paresis of the left side of the face, the left pupil was larger than the right, and the left side of the face and chest and left arm were observed to be sweating profusely.

Upon December 20th, the patient was so drowsy, that it was difficult to arouse him, swallowing/

swallowing was difficult, and there was loss of control over the bladder and bowel. Upon December 21st, he was distinctly brighter. The ptosis was almost complete, and there was some divergent strabismus; the upward and downward movement of the eyes was abolished, and the lateral movements were very defective. On looking to the left, the right eye moved very little beyond the middle line, while on looking to the right, the left eye moved over rather better, but tended to swing back towards the middle line. There were marked, fairly rapid nystagmoid movements on looking in all directions. The pupils were considerably dilated, the left being larger than the right, and both being practically immobile to light. A blood examination showed a slight leucocytosis, the leucocytes numbering 11,100. The differential count was as follows:-

Polymorphs	68%
Lymphocytes	22%
Large mononuclears	8%
Eosinophiles	2%

Upon December 28th, it is noted that he was still very drowsy, lying on his back all day, rarely attempting to move, and hardly ever making a spontaneous remark. The limbs, it was observed, were retained in any position in which they were placed. This had been a striking feature since admission. Upon December 27th, the patient was muttering to himself in a semi-coherent way, constantly giving orders to his men. It was necessary to speak loudly to him to wake him, but when asked a question, the delirium immediately ceased, and he answered intelligently. He stated that he had not been troubled with dreams. When asked as to how he felt, his reply always was 'quite well'. He appeared to have no discomfort. Last evening he attempted to get out of bed.

The results of the examinations of the Blood, & cerebro-spinal fluid, made from time to time, and for the most part by Captain James Miller were as follows:-

The cerebrospinal fluid when examined on December 14th, 1918, was found to be quite clear, the only cells found being a few lymphocytes; cultures made only for meningococci were sterile. A second/

second examination upon March 19th, 1919, shewed a clear fluid, a few lymphocytes being present. Wassermann complete negative: anaerobic cultures negative.

Diphtheroid bacilli were found in the cerebro-spinal fluid (~~See Appendix~~). These bacilli only shewed a small percentage Neisser positive, otherwise they resembled a true diphtheria; not tested on animals.

Blood culture gave no growth after 48 hours incubation. Wassermann on serum "complete negative": throat showed diphtheroids in considerable numbers, but these were not subjected to special tests. They were Neisser negative, but showed irregularity of staining. Widal shewed a trace of agglutination with B. typhosis, but no more than would be accounted for by inoculation. Faeces showed no evidence of pathogenic germs.

December 28th. The effect of cocaine on the pupil was tested. Two drops of a 4% cocaine solution was dropped into both eyes. After fifteen minutes both pupils were obviously dilating and equal in size: after twenty-five minutes only a very narrow margin of iris was to be seen.

December 29th. The left eye cannot be opened at all, while on the right side the lids can only be separated by about one eighth of an inch.

December 31st. He was rather restless, and for a short time did not seem to realise where he was, and attempted to get out of bed.

There was comparatively little change in the patient's condition by the middle of March 1919.

The iodides, Fowler's solution and strychnine were given a thorough trial in this case. The quantity given was increased up to full doses, and the result carefully observed. From none of the drugs, however, was it possible to say that definite benefit had been produced, unless possibly in the case of strychnine, which was given hypodermically.

REMARKS. This case is of interest as an example/
~~example~~

example of the typical clinical picture.

Among points of interest are the onset during convalescence from an attack of influenza, the almost complete ophthalmoplegia, and the persistence of the symptoms.

CASE III. Mr. B., a Colliery Manager, aged about 45, was seen in consultation at Methil on December 21st, 1918.

The patient stated that he had always been a particularly robust man, in no way nervous, and a life-long abstainer. Upon December 11th, he first noticed a severe pain in the left hand and forearm, which he stated came on without cause and extended into all the fingers and the thumb. The patient's medical attendant who saw him that day, could find nothing to account for the pain which became worse during the next two or three days, so much so that on two occasions morphia had to be given hypodermically. He had some headache, which was not, however, severe, and vomited a great deal for a day or two. A day or two later, he had some pain in the right hand and also round the abdomen about the level of the umbilicus, and more particularly on the left side. He also complained of some pain in the left leg, particularly behind the knee. On December 19th, he began to wander mentally, and was constantly talking of his work. The temperature was 99.5°. During these two days he was said to have been very drowsy.

When examined upon 21st December, the patient was quite clear mentally and gave a good account of his symptoms. The temperature was 100°, the pulse was 94, of good volume and regular, and the blood pressure appeared to be about normal. There was a very marked, fine, horizontal nystagmus on looking to either side. He stated that he had not seen double, nor was diplopia demonstrated. There was neither ptosis nor squint. The pupils were equal in size and not dilated, the left appeared to be a little sluggish to light.

No/

No facial weakness was observed. The tongue was rather dry and slightly tremulous. For some days he had had no appetite. The hands were tremulous. No paresis was detected. There was nothing abnormal about the reflexes. When the right leg was extended and then flexed upon the abdomen at the hip, he complained of some pain behind the knee. There had been no trouble with micturition, but the bowels were constipated. The abdomen was distended, there was no local tenderness, no splenic enlargement, and no skin rash. The heart and lungs were healthy.

December 23rd. The temperature was 100.5°, he was distinctly less tremulous, but there was a very distinct right-sided facial paresis.

December 29th. The temperature had been normal since December 23rd. There was a complete paralysis of the right side of the face, and the facial muscles did not respond to Faradism. He complained of what he described as massive pains, which shot up from the heels to the thighs. The arms he stated, felt very heavy, but no definite weakness was detected on examination.

The knee and ankle jerks were present and equal and the plantar reflexes were of the flexor type. The calf muscles were somewhat tender on pressure. The abdominal reflexes were absent; no abdominal tenderness or spots. The splenic dulness appeared to be enlarged, but the spleen was not palpable.

This patient wrote early in March to say that he was feeling practically well, excepting for the pains in the limbs, which still continued to trouble him. The facial paralysis had completely recovered.

REMARKS. Of special interest in this typical case are the onset with pain in the hand and arm, the persistent pain in the limbs, the late appearance of the facial paralysis.

CASE IV. Mr. R., aged 60. Seen in consultation
on May 1st, 1918.

This patient had been seen by the writer two or three years previously on account of a pressure neuritis of the musculo-spiral nerve. Some years prior to this, he had had an exactly similar condition in the opposite arm, brought about in the same way.

The patient's medical man stated that he had been consulted three weeks previously, on account of diplopia, giddiness when walking, and a pain above the right eye, which was at times very severe. On examination, he found, that the diplopia corresponded to a paresis of the fourth nerve, and he noted some tremor of the hands. Upon April 15th the patient was restless, complained of great thirst, and the pain above the eye was particularly severe. He had no desire for food and was constipated. Upon April 18th, the pulse was 110, the temperature 98.4°, and he was rather drowsy. Articulation was somewhat indistinct. He complained of great thirst and the tongue was very tremulous. He had hallucinations, imagining there were people in the room. The left side of the face was paralysed. He continued to become more drowsy during the next two or three days, and was said to be delirious at times. Marked nystagmus was observed. There had, at no time, been any difficulty in passing water, nor had the patient vomited.

On examination, upon 1st May, there was but little drowsiness. There was no ptosis, squint or paresis of the ocular muscles. The pupils, which were not markedly dilated, were equal and reacted to light, perhaps a little sluggishly. The optic discs were healthy. There was definite nystagmus on lateral deviation of the eyes, and a marked weakness of both sides of the face, with a good deal of tremor of the face when the patient spoke. The tongue was dry. Articulation was distinct. There was some tremor of the hands, but otherwise nothing abnormal was detected, upon examining the extremities, with the exception of some hypersensitiveness of the calf muscles (the patient is practically an abstainer).

The/

The patient, it was subsequently ascertained made a complete recovery and by July was back at work.

REMARKS. This, which was the first case in which the writer made a definite diagnosis, is very typical.

CASE V. Mr. H., aged 59, a retired grocer. Seen in consultation at Crieff on 20th March, 1919.

The patient, a man of very nervous temperament, who had for some years past suffered from occasional attacks of bronchitis and taken a good deal of alcohol in his day, stated that early in January, he had had a feverish cold, which lasted for nearly a week. His medical man diagnosed a slight bronchial catarrh. There were no characteristic symptoms pointing to influenza, nor was there any influenza in the house. Headache, giddiness, vomiting and diplopia, were not complained of, and at no time had a squint or ptosis been observed. For a time the patient was very drowsy, and often delirious, constantly talking of his work; when in this state, however, he always replied quite sensibly when spoken to. The tongue was heavily furred, and the bowels very constipated, so that frequent enemata were required. He was very tremulous. Weakness of the right side of the face was noticed in the earlier days of his illness, and has persisted. Pronounced general weakness without any actual paralysis had been present all along. Latterly it had been remarked, that he was unduly emotional, sometimes laughing, sometimes weeping, without adequate cause.

When examined on March 20th, the patient appeared to be mentally quite alert. There was no drowsiness. Speech and articulation were unaffected. There was a definite paresis of the right side of the face and some tremor of the hands. There was neither ptosis, squint, nor nystagmus, and the ocular movements were satisfactory. The pupils were equal and responded to light, the optic discs were healthy. Vision and hearing were quite acute. The tongue was protruded straight. Although/

Although no definite paralysis was demonstrated, there was a pronounced degree of general weakness, so much so, that the patient could neither dress himself nor walk farther than the bathroom. There was no alteration in the reflexes. Apart from a moderate degree of emphysema, there was no evidence of disease of the thoracic or abdominal viscera.

REMARKS. This case is also typical.

CASE VI. W. B., aged 27, a Marine Stoker, was seen with Dr. Claude Ker at the City Hospital on January 14th, 1919.

The patient was taken ill on January 11, drowsiness, headache, and some febrile disturbance being the conspicuous features. He was sent to the City Hospital as a suspected case of cerebro-spinal meningitis.

Upon examination on January 14th, the temperature was 102°, while the pulse was rapid. The patient was in a very drowsy state. There had been no delirium and he expressed himself clearly and intelligently. Some pain in the back had been complained of, but no pain in the limbs. The face, as Dr. Ker remarked, was expressionless. There was a slight degree of ptosis, the right palpebral fissure being narrower than the left. He was sweating profusely over the left side of the face. The pupils were of medium size, equal, and reacted fairly actively to light and on accommodation. There was no conjunctivitis, and no squint, nor was there a history of diplopia. The ocular movements were a little defective, for though there was no definite limitation, there was a tendency for the eyes to swing back towards the middle line, when an attempt was made to maintain them in the position of extreme lateral deviation. Although there was no true nystagmus, a little unsteadiness of the eyes was noted, particularly when the patient looked downwards. When the patient spoke there was practically no movement of the face, with the exception of the lips. The eyes were opened rather more easily than they should be, and when asked to raise the upper lip and show the teeth/

teeth, the movement was carried out in a lazy way. On speaking, some unsteadiness of the facial musculature was noticed. The tongue was extremely dry and tremulous. Articulation was somewhat indistinct. There was no history of discharge from the ears or nose, nor had the patient suffered from a sore throat. The hands were not tremulous and the grasp was good on both sides. There was no weakness or rigidity of the lower limbs, and no Kernig. The abdominal reflexes were absent, the knee jerks subnormal, and the plantar reflexes indefinite. There had been neither difficulty in passing water nor incontinence. The bowels had been very constipated. The heart sounds were closed and there was no dilatation. Nothing abnormal was noted in the lungs or abdomen. The urine contained no albumen. A scarlatinal rash noted yesterday was, in Dr. Ker's opinion, probably to be explained by an enema.

This patient died upon February 3rd (?) A Post-mortem was obtained (See second case referred to by Dr. MILLER in the section on pathology, page 102).

REMARKS. This is a typical case. The patient was taken ill while on a Battleship stationed at the time in the Forth, and it is of interest to note that there were a number of cases of influenza on board at the time.

CASE VII. Mr. M., a Solicitor, aged about 55, seen in consultation at Carlisle on 23rd February, 1919.

The patient, an active business man, had, with the exception of several attacks of acute rheumatism, previously enjoyed good health. During the war he had worked at exceptionally high pressure.

Three weeks previously he had been present at a public dinner and made a somewhat extraordinary speech, which had been commented upon by his friends. He stated that that evening he had had/

had one whisky and soda, and one or two glasses of burgundy. He walked home and the night was cold. The following morning, he complained of feeling light in the head, he saw double and was, his wife stated, exceptionally sleepy. On looking back, the patient stated, that he remembered some two or three days prior to this having given his head a rather forcible blow against the mantelpiece, while putting coal on the fire. He was a little dazed, for a few minutes in consequence, and wondered whether this might have been the cause of his illness. Upon February 14th, he went to London on business and returned to Carlisle on Wednesday the 19th, his doctor saw him first on the 20th. Excepting for some pain over the right side of his head for a day or two, some three weeks previously, he had had no headache, nor had he vomited. He had not had influenza recently, nor had there been any cases of influenza in the house, although there was a good deal in Carlisle at the time.

When seen by his medical attendant on February 20th, he was in a drowsy state, and somewhat delirious, constantly resuming his after-dinner speech. There was a good deal of tremor, and the patient was constantly plucking at the bed-clothes. He was, however, perfectly collected when spoken to. The temperature was normal, the pulse just over 70, and the tongue dry. He stated that he saw double on looking to the left. There was no defect of the ocular movements and no nystagmus. The pupils appeared to be immobile to light. There was no evidence of paralysis and no alteration in the reflexes. The urine was normal. The following day, the temperature was 101°. From February 19th to 21st, he passed no urine and yet the bladder was not distended. The bowels were constipated.

When examined on February 23rd, the patient was distinctly drowsy, though mentally alert. The temperature was normal, the pulse rate about 80. The tongue was dry and the patient stated that the mouth had felt dry since the beginning of his illness. Articulation was slightly thick. Diplopia was complained of, on looking both to the right and left, there was, however, no demonstrable ocular paresis. A few nystagmoid movements were observed on looking to either side, and well marked vertical nystagmus when the eyes were directed upwards, similar movements, though less marked, being observed on/

on looking down. There was some drooping of both eyelids, which, according to the patient's wife, was natural to him, although she admitted, that her husband had constantly of late presented a sleepy appearance, which was quite unlike him. The patient lay with his eyes half closed, although he could open them perfectly. He stated that he kept the eyes closed for the reasons that the lids felt heavy and that he found the light rather trying. The pupils were on the small side, the right being rather smaller than the left; both reacted very poorly to light. There was no hemianopia and no optic neuritis. There was no weakness of the facial muscles and no definite immobility, nor had there been any difficulty in swallowing. The grasp was quite good on both sides, but the hands were somewhat tremulous. No weakness of the lower limbs was detected. There was no tenderness of the calf muscles. The arm jerks and abdominal reflexes were absent, the knee jerks very sluggish, while the plantar reflexes were of the flexor type. The heart was not enlarged, the sounds were pure, and the blood pressure was 115. The urine was stated to contain no albumen.

REMARKS. The above description might suggest the possibility of an alcoholic polyneuritis. The patient was, however, a man of most abstemious habits, and the lethargic state and ocular palsies, place the diagnosis beyond doubt.

CASE VIII. Mrs. Y., aged 45, was seen in consultation on July 8th, 1918.

The patient lived with her husband and three daughters. A fortnight previously one of the daughters had had a typical attack of influenza. Five years before, Mrs. Y. was said to have been troubled with symptoms suggestive of disease of the spine. The spine was X-rayed, but the radiograms, which were seen by the writer, showed no evidence of bone disease.

A fortnight previously the patient, who had been in good health up to that time, complained of feeling tired, drowsy, and constantly sick, though she did not vomit. A week later she complained of some headache, and about this time the hands were noticed to be tremulous. Upon July 5th, she was delirious, the delirium persisting for two or three days. The temperature at this time was raised, the maximum elevation being 102°. Upon July 7th, diplopia was complained of for the first time.

When examined upon July 8th, the patient was in a somnolent condition. She looked, indeed, semicomatose, though she responded when spoken to. There was pronounced bilateral ptosis. The pupils were rather small and unequal. There was a slight divergent strabismus. The upward movement of the eyes was impaired, the downward movement completely lost, while on lateral movement, marked weakness of both internal recti was demonstrated. A distinct bilateral paresis of the face was present. The arms were slightly rigid, and there was some stiffness of the retrocolic muscles, though no head retraction. Some rigidity of the legs was also observed, and there was a definite Kernig's sign, rather more marked on the left side than on the right. The knee jerks were diminished and the plantar reflexes flexion. A careful examination of the lungs failed to elicit any signs of disease. The heart was normal. There were no enlarged glands, and nothing of note was detected in the abdomen. The urine was said to contain no albumen. On lumbar puncture, a perfectly clear fluid, which was not under pressure, and which subsequent examination showed contained no increase of cells, was obtained. Cultures from the cerebro-spinal fluid showed no growth.

The patient died, it appears, ten days later, the state of coma gradually deepening. Permission for an autopsy was refused.

REMARKS. At first sight the question arose whether this might not be a case of tuberculous meningitis, a possibility which was accentuated by the history of suspected disease of the spine. The negative/

negative radiograms, the absence of evidence of tubercle elsewhere, the fact that the patient had been in good health up to the time of onset, the character of the symptoms as a whole, and above all the examination of the cerebrospinal fluid justified the exclusion of this possibility. It is of interest to note that the patient's daughter suffered from influenza, a fortnight before she was taken ill.

CASE IX. M.A.R., a spinster, aged 44, and a Tweed-Darner by occupation, was seen by the writer at the Royal Infirmary upon February 6th, 1919, on the recommendation of her medical attendant.

The patient lived by herself in a one-roomed house. She stated that she seldom tasted alcohol. A sister had died of consumption.

Upon February 3rd, she stated that she had had a headache and that she vomited. The next day she went to her work, but had to give up she felt so ill. She was feverish, complained of pain down the back of the neck, and saw double.

When examined upon February 7th, the day after her admission to Ward 33, she was in a drowsy, semicomatose state. The temperature was 99.40°, the pulse rate 86. The previous night there had been some delirium. She talked of her work and was with difficulty restrained from getting out of bed and putting on her clothes. There was some drooping of the eyelids, especially the right. The right pupil was larger than the left; both were of medium size, regular in outline, and almost immobile to light. There was no strabismus or nystagmus. The diplopia had passed off the previous day. The face appeared to be distinctly immobile, although no definite paresis/

paresis was detected on further examination. The optic discs presented a healthy appearance. There was no tremor or paralysis of the limbs. The knee jerks were only obtained with difficulty, the right being a little more active than the left. The ankle jerks were present and there was a bilateral extensor response. There was no Kernig or neck rigidity. The tongue was somewhat dry and the bowels markedly constipated. There had been incontinence of urine during the previous night. The bladder was not distended. The wall of the radial artery was not palpable, and the systolic pressure was 144. No evidence of disease was found elsewhere. t

The urine examined the same day contained no albumen but both sugar and acetone were stated to have been present. Repeated examinations on subsequent dates showed, however, no trace of either. The cerebrospinal fluid was perfectly clear and was stated to contain no cellular elements. The Wassermann reaction on the blood and cerebrospinal fluid was definitely negative.

2
Upon March 30th, the patient was in very much the same condition as on admission.

The writer has notes of a number of other cases exemplifying this type, but since the features are very similar to those above described, it is not proposed to include the case records.

TYPE II. characterised by pronounced lethargy
with the usual febrile disturbance while
the focal brain symptoms are comparatively
insignificant or absent.

CASE X. Mrs M., a widow, aged 47, seen in consultation on 19th August, 1918.

The patient, a woman of somewhat nervous temperament has never been very robust. As a child she suffered from tuberculous disease of the elbow. Menstruation ceased two years ago.

On the night of August 16th, Mrs M. went to bed feeling quite well. The following morning when she awoke she said she felt 'funny' and when seen by her doctor later in the day, she was in a drowsy, semi-dazed condition. The temperature was 99°. She complained of no pain. The patient's medical attendant was inclined to regard the case as an atypical influenza. The following day she was still more drowsy, the temperature was not raised and no abnormal physical signs were detected.

On examination, the patient was found to be very drowsy. She was very slow in grasping the meaning of questions and commands. There was, however, no aphasia or dysarthria, and her replies were intelligent. She had, it was stated, volunteered no spontaneous remark during the previous few days. The temperature was normal, the pulse 66 and regular. There was a slight degree of ptosis on the left side. The left pupil which was rather larger than the right, reacted poorly to light. There was no nystagmus or squint, but the movement of the left eye, when the patient looked to the right side was a little defective. The Optic discs were healthy. A patch of herpes was present on the upper lip, no facial weakness, no dysphagia. The tongue was moist and fairly clean. There was a very slight bilateral Kernig, no neck rigidity, weakness of the limbs or tremor. The knee jerks were present, equal and not exaggerated, the plantar reflexes flexion. The heart and lungs were healthy. There were two or three papules on the skin of the abdomen which suggested the possibility of enteric, but none elsewhere. There was no abdominal distension, tenderness or gurgling. The spleen was not palpable. There was no sphincter trouble. The urine contained neither albumen or sugar. The bowels had been very constipated.

On August 29th, the patient was seen again. Until two or three days previously, she had remained much in the same condition. The drowsiness, which had been rather less was now very pronounced, amounting to a state of stupor. There were no further cerebral symptoms. The Widal was negative both for Typhoid and Paratyphoid. The temperature had occasionally been up to 100° or 100.5°. There had been some twitching of/

of the face, right leg, and left arm. She had complained of no headache, nor had she vomited; there was no definite Kernig and nothing abnormal was detected in the chest or abdomen. The spots on the abdomen had disappeared. On lumbar puncture the cerebro-spinal fluid was not under pressure. It was quite clear and there was no increase of cells.

Death occurred on 3rd September. Before death a pronounced divergent strabismus and some tremor of one leg and the opposite arm was noted. Permission for a Post-mortem examination was not obtained.

REMARKS. This case was characterised by pronounced drowsiness, febrile disturbance and slight focal brain symptoms. The diagnosis was based largely upon the exclusion of other possibilities. Enteric fever was excluded on account of the absence of abdominal symptoms and splenic enlargement, the negative blood examination and the sudden onset ^{with} of the ocular paresis, while the absence of Kernig and neck rigidity, and the condition of the cerebrospinal fluid, justified the exclusion of the various forms of meningitis.

CASE XI. Miss C. aged 24, seen in consultation on December 10th, 1918.

The patient who was stated to be of a rather quiet and retiring disposition had been driving a motor lorry for the A.S.C. During the previous month, she had had a good deal of trouble. Three or four weeks previously her best friend had died of influenza, the friend's mother dying a day or two later from the same cause. She was taken to see her friend's body after death. This incident had apparently made a great impression upon her. A fortnight previously, and since that time, her mother/

mother stated she had been unusually low-spirited, irritable and reserved. She was ordered to go to another part of the country. This was a great disappointment to her, since she had just become accustomed to a new car which she was not to take with her. It was about this time that she began to complain of headache which was generalised and somewhat severe for a few days. Upon one occasion she had vomited. For three or four days she had complained of a stiff feeling in the legs.

On examination upon December 10th, the patient was in rather a dull and stupid condition, and was only with some difficulty persuaded to respond to questions. The temperature was normal, the pulse rate a little rapid. She was able to walk about, but the gait was a little shuffling. No weakness was detected in the limbs nor was there any tremor. The knee-jerks were somewhat increased and there was a bilateral ankle clonus but Babinski's sign was definitely negative. There was no Kernig. The pupils were equal. There was no nystagmus, and the optic discs were normal. The examination was otherwise negative.

To his record of the case, the writer appended the following note:-

"There is certainly nothing that I can put my finger on certainly indicative of an organic process. My impression is that the condition is a functional one and that she will make good progress; at the same time for a few days one cannot help feeling a little anxious about her".

The following day the patient's medical attendant telephoned the writer to say that pronounced symptoms had developed which were suspicious of a meningitis, together with a high temperature, and upon December 13th, she was admitted to the City Hospital as a suspected cerebrospinal meningitis. According to information derived from Dr. Claude B. Ker, the patient was "very drowsy; tongue very dry: no true Kernig: legs very rigid with toes pointed: pupils very sluggish but equal: no ptosis or nystagmus: lumbar puncture showed a perfectly clear fluid". The patient died two days later, but permission for a post-mortem examination was not obtained.

REMARKS. This case, as will be seen was at first erroneously diagnosed as probably functional.

CASE/

CASE XII. Miss B. aged about 60. Seen in consultation at Juniper Green on 28th December 1918

The illness dates back for about three weeks. The onset was characterised by some slight febrile disturbance, ^{and} a pain in the right leg which was regarded as a sciatica. This pain, which was severe at first had improved greatly during the previous week. The patient had complained of want of appetite, the bowels had been very constipated: she had been drowsy and somnolent. There had been no cases of influenza in the house.

When examined upon December 28th, the patient was in a distinctly drowsy state. The temperature was 98.2° the pulse was 80 and regular. The abdomen which was somewhat distended, was not tender. There was no typhoid rash and no splenic enlargement. There were a few crepitations at the bases of both lungs, but the breath sounds were vesicular. Some pain was complained of when the limb was moved, but movement at all the joints was quite free. Pain behind the hip was complained of, when the leg was extended on the trunk. There was no ptosis, strabismus or nystagmus. The pupils were equal. The knee and ankle-jerks were present and equal, the plantar reflexes flexion. There was no albumen in the urine.

Blood was withdrawn for a Widal, but the examination was definitely negative. The patient, it was subsequently ascertained, gradually became more comatose and died a few days later.

REMARKS. Possible exception may be taken to the inclusion of this case as an instance of encephalitis lethargica. That the condition was an infective febrile process, there could be no doubt. Influenza, enteric fever and encephalitis lethargica were the three suggested possibilities. The initial symptoms were not like an influenza, nor was the course of the case suggestive of this disease. There were/

were no symptoms characteristic of typhoid fever, no diarrhoeas, splenic enlargement or spots. The patient's medical attendant stated that there was no case of typhoid fever in the district, so far as he knew, and he was so satisfied that this was not an instance of the disease that he had not had the blood examined for a Widal reaction. If the drowsy state was to be accounted for by an encephalitis, there were no symptoms indicative of a focal brain lesion and the diagnosis must be arrived at by exclusion. The blood examination which gave a negative Widal both against typhoid and paratyphoid, was weighty evidence against this disease.

TYPE III. characterised by well marked focal symptoms, while the lethargy and febrile disturbance are so slight that they may escape detection.

CASE XIII. Miss R. aged 40 (?) seen in consultation on January 30th, 1919

The patient a Farmer's daughter, stated that she had always been robust. Just before the New Year she had had a 'cold'. There were no cases of influenza in the house and her symptoms which seemed to be those of an ordinary nasal catarrh, did not suggest an influenzal infection. Sometime during the third week of January, she stated that when she rose from bed one morning she felt giddy, and saw double. Next day she stated that she vomited and had a very slight headache 'not worth mentioning' over the vertex of the head. At no time had she felt feverish. Her sister stated that she was a little drowsy for a week or ten days but continued as usual with her work. There was no delirium. The vertigo and diplopia only continued for three days. About a week after the giddiness and vertigo came on, her face was noticed/

noticed to be 'twisted'. She said she had been unable to read or sew since the onset of her illness. The bowels, too, had been very constipated.

When examined upon January 30th, the patient said she felt quite well and that her one trouble was the paralysis of the face. There was a distinct drooping of both upper eyelids, which was equal in degree. The patient's sister corroborated the impression that there had been no drooping of the lids prior to the present illness to which the ptosis must consequently be attributed. There was no strabismus, but the movement of the right eye to the left was certainly a little defective and the nystagmus most pronounced in the right eye when she looked in this direction, was observed. On lateral deviation to either side there was a tendency for the eyes to swing back towards the middle line. The pupils were equal and of medium size, but the reaction of both to light was not as brisk as it should have been. There was a complete paralysis of the right side of the face. There was no weakness of the jaw muscles, dysphagia, paresis or tremor of the tongue and no evidence of loss of power in the limbs was detected. The patient stated that she could walk a considerable distance without feeling tired, and that she could use her arms as well as ever. The reflexes were unaltered. There was no evidence of disease elsewhere. When seen again, upon February 4th, she was able to close the right eye and raise the right eyebrow slightly. The lower part of the face was, however, quite immobile, except possibly for a slight contraction when she smiled.

REMARKS. This case presented a complete unilateral facial palsy with paresis of the ocular muscles, while the general symptoms were evidently slight and unusually transient. The condition of the face was especially interesting.

CASE XIV. Miss W. aged 20, an Arts student, was seen in consultation at Kirkcaldy on January 28th, 1919.

The patient a particularly clever girl,
had/

had for the past year been living in Edinburgh attending an Arts course. She had enjoyed excellent health. In November she had what appears to have been a typical attack of influenza, from which she was stated to have made a good recovery.

Upon December 28th, she complained of giddiness and vomiting. These symptoms had persisted since. Her bowels had been very constipated. There had been no headache nor had any febrile disturbance been noted. She was said to have been slightly drowsy.

On examination the patient was found to be a well developed, healthy looking girl. She was lying in bed, afraid to lift her head off the pillow, since any attempt to do so always, she stated, brought on giddiness and vomiting. There was slight drooping of the right upper lid, and the movement of the right internal rectus was somewhat defective. Very marked nystagmus was observed on lateral deviation of the eyes, while on looking upwards, vertical nystagmus was observed. The pupils were equal and responded well to light. Both vision and hearing were acute. The fundus oculi presented a normal appearance. There was no facial paresis and no definite weakness of the limbs, no Kernig and no neck rigidity. The knee-jerks were somewhat brisk and equal. There was no ankle clonus. An extensor response was obtained from the ball of the great toe on either side, but not from other parts of the plantar surface. The abdominal reflexes were present. Nothing abnormal was detected in the chest or abdomen. The urine contained no albumen.

REMARKS. The diagnosis in this case obviously lay between encephalitis lethargica and disseminated sclerosis. It seemed justifiable to exclude a tuberculous meningitis with certainty, in view of the patient's satisfactory general condition, the absence of any signs of tubercle elsewhere, the absence of temperature, neck rigidity or Kernig, and the acute onset. A lumbar puncture was not carried out./

out. The acute onset with vertigo and vomiting in a girl who had not previously exhibited any nervous manifestations, all pointed towards encephalitis lethargica as the most probable diagnosis.

TYPE IV. An Abortive Type characterised by the transient duration of the symptoms, which clear up entirely or almost completely in the course of two or three weeks.

Two instances in point are as follows:-

CASE XV. Sergt.C.H., aged 23, 5th Reserve Scottish Rifles, admitted to the 2nd Scottish General Hospital under the writer's care on 31st May 1918.

The patient stated that he went to France on December 3rd, 1914, and served continuously there till March 1917, when he was evacuated to England with pleurisy. Since April 11th, when he was discharged from Hospital, he stated that he had remained well.

Upon May 14th, or thereabouts, he was admitted to Hospital from the camp at Kinross, where he was at the time stationed, complaining of intense drowsiness and some headache, which had not, however, been severe. This condition had continued up to the date of his admission to Craigleith.

When examined on May 21st, his one complaint was of drowsiness. He stated that he felt inclined to go to sleep at all times and could only keep himself awake by a great effort. The headache of which he had previously complained, had almost gone. While the writer was examining the patient, his head dropped forward on his chest and he began to nod. He moved about in a slow/

slow lethargic fashion, and although he answered questions quickly, he had a somewhat dazed and uninterested appearance. His mind was quite clear. He stated that the onset of the drowsiness was preceded by double vision at a distance and that he had been rather 'bleary-eyed' since the commencement of his illness. The diplopia had passed off. His acuity of vision was, unfortunately, not tested. The optic discs presented a healthy appearance. The ocular movements were satisfactory. There was no nystagmus and the pupils reacted normally to light. The tongue and hands were somewhat tremulous. The reflexes showed no abnormality, and no objective sensory disturbance was detected. There ~~was~~ ^{were} no abnormal cardiovascular signs and the urine contained no albumen. The Wasserman reaction on the blood serum was definitely negative. By June 9th, the patient was much less drowsy and on June 16th he had quite recovered and was discharged from Hospital fit for duty.

REMARKS. The symptomatology of this case leaves no doubt as to its nature. Points of special interest are the pronounced drowsiness, the absence of focal brain symptoms, apart from the transient diplopia, and the rapidity with which the symptoms cleared up.

The following case in which the diagnosis is necessarily based on the patient's statements and is consequently open to criticism, is, in the writer's opinion, almost certainly an example of encephalitis lethargica of the abortive type.

CASE/

CASE XVI. Lance Corporal J.A.R., aged 32, of the R.A.S.C., was seen on the recommendation of Sir George Berry at Craigleith upon December 27th, 1918.

The patient, a shoe merchant, and a very intelligent man stated that he had always been healthy and that he went to France in March 1918.

Upon October 21st, he stated that he went to bed about 10.p.m., feeling in his usual good health, but that when he awoke in the morning he found that he was unable to raise his eyelids, though otherwise he felt well. When seen that day he stated that the Medical Officer on raising the lids, found that he had a squint, the right eye being directed outwards. The patient further stated that he was somewhat unsteady on his legs and that the legs felt weak. Upon waking on October 23rd, he found that he was able to raise the lids slightly, but could not keep them up. By Monday 25th October, he was able to open the eyes fairly well, but found that he was seeing double. The doctor gave him to understand that the movements of the eyes were satisfactory with the exception of the internal muscle of the right eye (? the internal rectus). The patient stated that at the commencement of his illness, he had had a good deal of headache, especially at the back of the eyes and notably on the right side. There had been no vomiting or giddiness and as far as he was aware, no febrile disturbance, nor had he been drowsy. The diplopia had persisted. Sir George Berry found no obvious weakness of the ocular muscles, but noted that "the diplopia of which the patient complains is characteristic of an internal rectus paresis".

The writer's examination was entirely negative. The patient was feeling perfectly well in every way apart from the diplopia.

REMARKS. This is a most interesting case. That the paralysis of the internal rectus muscle was attributable to an organic cause, there can be no/

no question. The patient was a most intelligent man, and, assuming his statements to have been correct, it is clear that he suffered from a transient or pronounced complete bilateral ptosis, which passed in the course of a few days. The lesion must have been a consequence of an abortive encephalitis. What alternative diagnosis can be advanced to explain the facts?

TYPE V. characterised by a physiognomy which closely simulates Paralysis Agitans.

CASE XVII. Private George S., R.D.C., aged 40, was admitted to Hospital under the writer's care, on February 22nd 1919.

Sixteen years previously, the patient had had a haemoptysis which has recurred on two or three occasions since. Soon after enlisting in October 1916, he "went sick" for fourteen days with palpitation and shortness of breath, evidently due to heart strain, brought on by his military duties. Otherwise he stated that he had enjoyed good health.

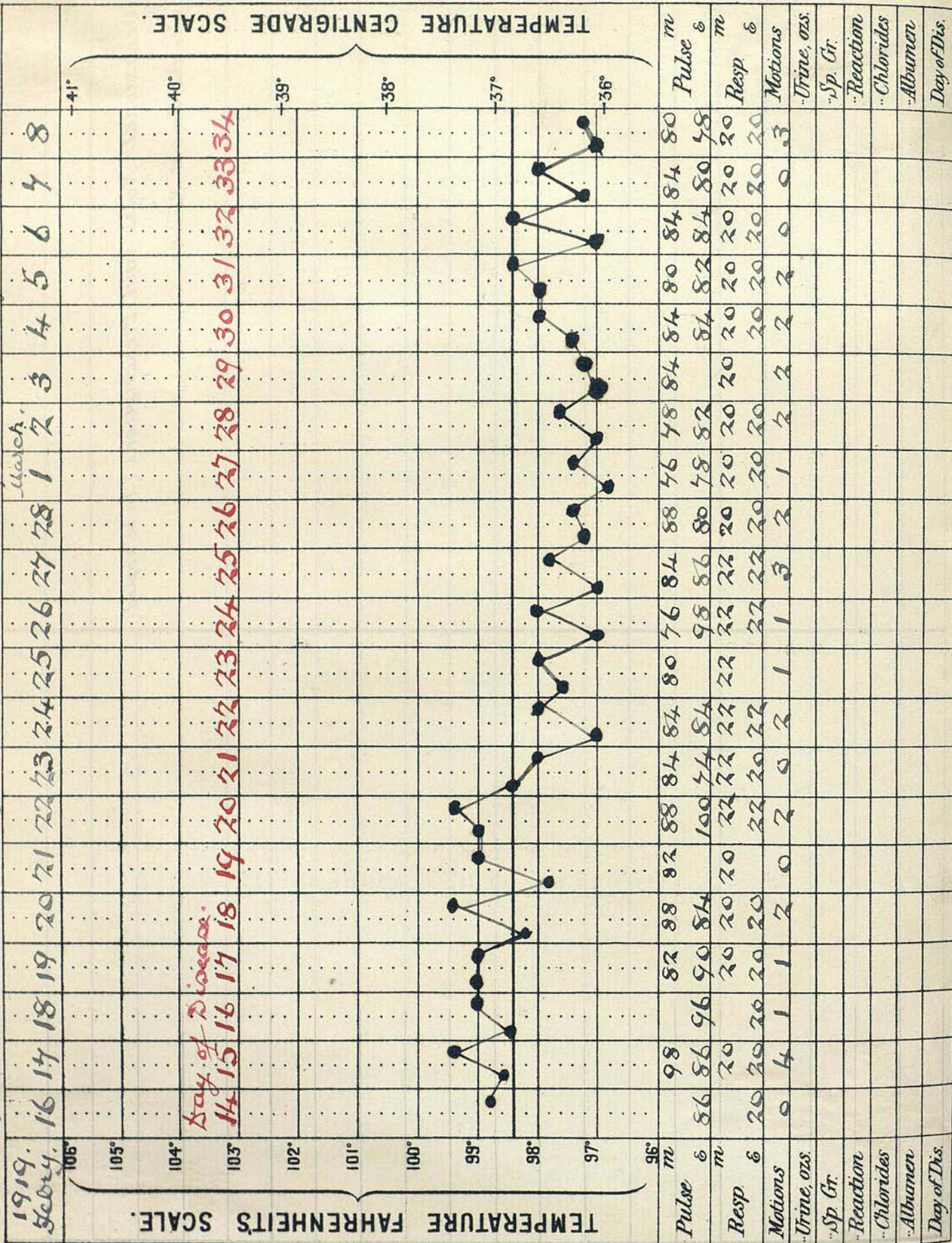
Upon February 3rd, 1919, while in camp at Stobo in Peeblesshire, he felt shivery and feverish. On the 6th he complained of some frontal headache, and on the 8th he saw double: the diplopia lasting for three days. Since this time his vision had been blurred. For a few days previously, the bowels had been very constipated. The Medical Officer told him that he had a slight attack of influenza. On enquiry, it appeared that the patient had neither pain in his limbs nor catarrhal symptoms and that there had been no cases of influenza in the camp. Upon February 12th, he was admitted to the Surgical Wards of the/

(Case XLII, p. 85.)

Name Pte. S. S.

Age 40.

Disease Encephalitis Lethargica. Result



the 2nd Scottish General Hospital with retention of urine. On admission, he was complaining of dull headache, dimness of vision and some shaking of the right hand, which he had first noticed the previous day. During the ten days he was in the Surgical Ward, he is said to have been very drowsy and his temperature ranged from 98° to 99.6°. The tremor of the hand became more pronounced.

Upon February 22nd, the patient was found to be mentally alert. The face was typically mask-like recalling the faces in paralysis agitans. There was neither ptosis nor squint. The left pupil was a shade larger than the right and both responded very poorly to light. Nystagmoid movements were observed when the patient looked to either side. The tongue was moist and slightly tremulous. The attitude of the right arm was striking. It was flexed at a right angle at the elbow, the fingers being in the writing position fully extended at the interphalangeal joints, and adducted and flexed to almost a right angle at the metacarpo-phalangeal joints. There was, in addition, a constant rhythmical tremor of the right arm, the movement being essentially one of alternate supination and pronation. The tremor was not accentuated by volitional effort. No tremor was observed elsewhere. There was no definite weakness of the limbs. The reflexes presented no abnormality. Beyond some slight impairment of the percussion note and somewhat harsh breath sounds, at the apex of the right lung, nothing abnormal was noted on examination of the chest or abdomen. The urine contained a few pus cells.

REMARKS. The Report from the Pathological Laboratory (Dr. James Miller) was as follows:-

"Cerebrospinal fluid (reported 16.3.19): clear
 "but with minute flocculi; centrifuged fluid
 "shows cells in considerable numbers, lymphocytes
 "predominated but there were a few polymorphs.
 "Culture 24 hours on blood serum showed two colonies of Neisser positive diphtheroids, also
 "present/

"present in broth after 48 hours; anaerobic cultures negative.

For characters of diphtheroids see page 108.

"Sputum: on several occasions showed numerous

"diphtheroids Neisser positive. These we always

"failed to culture. The accompanying organisms

"differed on each occasion.

"Throat swab (reported 7.3.19): on blood serum

"showed diphtheroids of Hoffmann's type.

"Naso-pharyngeal swab: no meningococci and no

"pharyngococci.

"Wasserman of cerebrospinal fluid and serum

"both negative.

"Widal (reported 7.3.19)

Typhoid bacilli agglutinated to 1:640 fine

Paratyphoid A. to 1: 640 fine

Paratyphoid B. to 1:1280 coarse.

"Faeces overgrown.

"Blood culture, completely sterile both aerobic

and anaerobic.

"Blood count:-

R.B.C. 5,700,000 Hb. 95%, W.B.C. 7,800

(Differential count:-

Polymorphs	62.6%
Large mononuclears	8.6%
Lymphocytes	26.3%
Eosinophiles	2%
Basophiles	0.3%.

The majority of the large mononuclears shew fine granulation.)

REMARKS/

REMARKS. The febrile onset, drowsiness, ocular paresis, etc., leave no doubt as to the diagnosis in this case. Unusual features are the attitude of the right hand and the tremor, which were in themselves indistinguishable from the appearances met with in a case of paralysis agitans, and are no doubt to be accounted for by a lesion involving the rubro-spinal tract. The facial appearance accentuated in a striking manner the resemblance to Parkinson's disease.

The presence of a Neisser positive diphtheroid in the cerebrospinal fluid and sputum will be referred to later. (~~See Appendix.~~)

CASE XVIII. Mr W.M., aged 30, a monotype operator, seen on February 6th 1919 on the recommendation of his medical attendant.

The patient stated that he had always been a fairly healthy man and that his present symptoms dated from December 12th when, after going to bed feeling well, he awakened with diplopia. A fortnight before he had had a 'cold in the head' but this had completely cleared up a week previously. With this cold he had had no fever, no headache or pains in the limbs nor were there any cases of influenza in the house. When seen by an oculist the same day, his eyelids were stated to droop slightly. By December 16th, the diplopia had passed off. He had had no headache nor had he vomited. Upon the following day, the 17th, he was said to have perspired profusely, and to have been feverish. By the 18th, the eyes were practically closed and upon this date, he began to be very/

very drowsy "sleeping all the time" and yet in his sleep he was constantly speaking of his work. He had to be wakened to be fed. The pronounced drowsiness lasted for a fortnight and then gradually passed off. The patient remembered little or nothing of this period. His speech was altered at this time. He stated that it was an effort to speak. Excess of saliva had recently been a troublesome symptom and this, together with an inability to hold his head up, because of weakness in the neck muscles, was his one complaint. After the drowsiness passed off, he stated, that he was left in a very nervous state.

When examined upon February 6th, there was no drowsiness or mental abnormality, his mental alertness, indeed, being in marked contrast with his appearance. His vision was impaired so that he had difficulty in reading, the letters running into one another. The pupils were small and equal. They contracted to light. The ocular movements were satisfactory and there was neither squint nor nystagmus. The physiognomy was very striking. The face was devoid of all expression. He walked with his head inclined forwards and the posture of the hands, which was very similar to that observed in cases of paralysis agitans, accentuated the resemblance to this disease. Although the eyes could be closed, it was possible to open them with comparative ease, the patient doing his best to resist. The movements of the lower part of the face were still more defective. The patient could no longer whistle, whereas he had been able to do so quite well before his illness. The tongue showed no abnormality, nor was there any difficulty in swallowing. The upper limbs, apart from the posture above referred to, which suggested a case of paralysis agitans, presented no abnormality. In particular there was no tremor. There was no obvious weakness of the lower limbs, nor did the reflexes show any alteration. Some desquamation was observed over the forehead, but not elsewhere. A few papules, probably due to the bromide which he had been taking were noted on the chest. Beyond a short systolic murmur heard over the apex beat of the heart, conducted towards the axilla and unaccompanied by any enlargement of the left ventricle, nothing of note was detected on physical examination.

the/

The systolic blood pressure was 145.

REMARKS. The resemblance presented by the Patient to a case of paralysis agitans without tremor was very striking.

TYPE VI. characterised by cerebellar ataxia as the prominent symptom. The following case is an example in point.

CASE XIX. Elisabeth H. aged 24, was seen by the writer in the Waiting Room of the Royal Infirmary on the recommendation of her medical attendant.

The patient stated that prior to the previous two months she had always been strong and healthy. She then noticed that her vision was defective, and that she had difficulty in reading. Two or three boils appeared over the sacrum about this time. Her sister who accompanied her, stated that some ten days previously, the patient became very drowsy. She was so drowsy that it was necessary to shake her in the morning to waken her, and they had to shake her in order to feed her. She went off into a sort of sleepy state, whenever she was left alone. The drowsiness had persisted, but had been much less pronounced during the past two days. The patient had not complained of headache, nor had she vomited.

On examination, no sign of organic disease of the nervous system or other organs, was detected, saving the facts that there was definite lateral nystagmus when the patient looked to either side, and vertical nystagmus on looking upwards, and that the pupils which were of medium size and equal reacted a little sluggishly to light. The acuity of vision was not tested. There was no squint. The ocular movements were satisfactory and the optic discs were healthy. The urine contained no albumen.

The opinion expressed in a letter to the/

to the patient's medical man, was as follows:-
 "The drowsy state and nystagmus in the absence
 "of other signs are very suggestive of encephali-
 "tis lethargica, and my opinion is that this is
 "the probable lesion".

The patient was subsequently admitted to Leith Hospital under the care of Dr. Matthew, to whom the writer's thanks are due for permission to examine her again on 20th January, 1919. The House Physician stated that on admission, she had been in a rather drowsy state and continued so for two or three days, that the temperature was normal, that upon August 24th, she was allowed to get up, but that a day or two later she became very ataxic with a tendency to stagger to the right; that for a time articulation was very indistinct, and there was great difficulty in swallowing; that she was very dull and that incontinence both of urine and faeces was of frequent occurrence; that the dull mental state gradually passed off; that she was, however, very emotional, giggling and weeping, so much so that it was difficult to examine her, and that on September 10th Dr. Sym examined the eyes, but apart from some congestion of the retinal veins, found nothing abnormal in the fundus.

When examined by the writer upon January 20th, 1919, the patient was bright and cheery, but somewhat emotional. The pupils were of medium size, equal and reacted to light. The ocular movements were good, but there was distinct nystagmus on looking to either side, less pronounced on looking up or down. There was very slight paresis of the left side of the face. Articulation was perfect. The tongue which was protruded straight was clean, moist and steady. The hands were slightly tremulous. The grasp was good. With the eyes closed, she missed the point of the nose by an inch or two with either hand and the movements were carried out somewhat unsteadily. The gait was somewhat ataxic and the incoordination was not increased when the eyes were closed. The abdominal reflexes were present and equal, but a little difficult to elicit. The tendon reflexes of the lower extremities and the plantar response showed no abnormality.

REMARKS. The diagnosis of encephalitis lethargica was beyond doubt in this case. Apart from the/

the drowsiness, ataxia was the predominant focal symptom. It might be argued, in view of the emotional instability, that the incoordination was of functional origin, but the impression obtained from the House Physician's description suggested, in the writer's opinion, a cerebellar ataxia. This was supported by the examination upon January 20th.

CASES/

CASES presenting a different SYMPTOMATOLOGY but
possibly due to the same
PATHOLOGICAL AGENT.

As has been mentioned, the writer has during the past few months met with a number of anomalous cases of an unfamiliar type in which the symptoms, referable either to the brain, spinal cord or peripheral nerves, did not conform to the clinical picture of encephalitis lethargica as above described, but which were evidently dependent upon an infective process, the nature of which was not apparent. The question arises whether these cases may not have been due to the same virus which is responsible for encephalitis lethargica. Lethargy was not a noticeable feature in these cases, but if the view adopted in this thesis, that the lethargic state is a focal mesencephalic symptom, dependent upon the interruption of afferent thalamic impulses is correct, the absence of this symptom merely indicates that the mesencephalon is not interfered with in such a way as to produce such an interruption. The tentative suggestion, that the symptoms in the cases presently to be referred to, may be caused by the same pathological virus, as are cases of encephalitis lethargica, is supported/

supported by the fact that in several symptoms dependent upon impairment of the ocular musculature were observed. It is quite possible that in the future intermediate cases may present themselves, the symptomatology of which may serve to bridge the gap.

Again, the detection of a causative agent common to encephalitis lethargica, and to these anomalous cases under consideration would place the relationship beyond doubt. Meanwhile, however, the available evidence can only be regarded as suggestive and not conclusive. Among several cases the writer has selected three, the details of which are as follows:-

A CEREBRAL TYPE characterised by symptoms which indicate a (FOCAL) LESION of the CEREBRUM.

MRS S. aged 43, was seen in consultation on
16th April 1918.

It was ascertained that the patient had been in the past a healthy woman. On the previous evening she left the room where she had been sitting, and was found a few minutes later lying on her face unconscious on the floor of the lavatory. She had made no complaint of feeling unwell nor had anything amiss been noticed. Her medical attendant, who saw her that evening found her in a semi-conscious state. She would not say a word when spoken to and was throwing herself about in a violent way. The pupils were equal. Some weakness of the left side of the face was noticed and the left conjunctival reflex was absent. The pulse was slow, about 50, and slightly irregular. No albumen was found in the urine which was drawn off by the catheter.

When/

When examined twenty hours after the onset of the symptoms above described, the patient was in a semi-dazed state, but she replied though in a somewhat disconnected way when spoken to. The temperature was not raised. Any attempt to move or examine the patient was resisted. The left pupil was rather larger than the right, both were regular and reacted to light. There was distinct paresis of the left side of the face and possibly a little weakness of the left arm; the left knee-jerk was increased and the left plantar reflex definitely extensor. There was no squint. The optic discs were healthy. It was impossible, on account of the patient's mental state, to examine the ocular movements, nor was it possible to ascertain with certainty the presence or absence of neck rigidity or Kernig's sign. The pulse rate was about 60. The blood pressure did not appear to be raised. The radial artery was not thickened. The cardiac apex was somewhat forcible and heaving but in the 5th space and nipple line. The heart sounds were closed. Nothing abnormal was detected in the lungs or abdomen, except for a tumour of some size in the region of the right kidney which from facts subsequently ascertained was probably a hydronephrosis. There was no suggestion of syphilis either in the family history or upon examination, nor was there any history of otitis.

REMARKS.

The nature of the lesion in this case was not clear to the writer. The fall had apparently been the consequence and not the cause of the symptoms. Embolism could be definitely excluded in the absence of any valvular affection. Again there was no evidence of disease of the blood vessels or kidneys. Yet the suddenness of the onset suggested a lesion of vascular origin. Haemorrhage into a tumour seemed to be improbable, since there was no history/

history of headache or vomiting, while in addition, there was no optic neuritis. The acute onset in an individual apparently perfectly well up to that time was opposed to a thrombosis, while the mode of onset, the absence of pyrexia and the hemiparesis were unlike. The cerebrospinal fluid was not examined. The after history of the case is interesting. The patient remained much in the same state, it seems, for several days and from that time steadily improved. Whether there was any febrile disturbance, the writer has been unable to ascertain. Two months later, the patient was going about as usual perfectly well. An encephalitis would certainly seem to be the most probable explanation of the facts.

A SPINAL TYPE characterised by SYMPTOMS which indicate a (FOCAL) LESION of the SPINAL CORD.

Mr.W. a baker, aged 37. Seen in consultation at Milnathort, upon March 17 1919.

With the exception of a severe attack of typhoid fever at the age of 17, and an attack of acute appendicitis some six years previously, the patient has had no previous illnesses. In December 1918, the patient had had a rather sharp attack of influenza from which he stated that he had quite recovered, when his present symptoms developed.

Upon March 10th, patient complained of feeling shivery and feverish and of pains throughout/

throughout the body but especially between the shoulders and in the arms. The following day, some slight weakness of the legs was noticed. Upon March 14th, the legs were said to be completely powerless, the knee-jerks being absent.

When examined upon March 17th, the patient stated that for several days he had been seeing double, when he looked to the left. No history of drowsiness was obtained. He looked ill, but the mind was quite clear. The temperature was 102.4° the pulse 124. There was a complete flaccid paralysis of both lower limbs with almost complete sensory loss up to a level about two inches above the umbilicus. The knee-jerks and plantar reflexes were absent. The bladder was distended and the patient was unable to pass water. The urine which had been drawn off regularly for the previous two days was said to contain some pus. No evidence of interference with the upper limbs was elicited. There was no paresis of the face. The ocular movements were not impaired and there was no ptosis, but marked nystagmus was observed on deviation of the eyes especially when the patient looked to the left, the movement of the right eye to the left being slightly defective. The pupils were equal and responded to light. A patch of herpes was noticed about the left angle of the mouth. No abnormal objective signs were found on examination of the thorax and abdomen, with the exception of the distension of the bladder above referred to. Venereal infection was denied.

REMARKS. This patient presented symptoms which clearly indicated the presence of an acute myelitis in the mid dorsal region of the spinal cord. Venereal infection was denied and the acute onset with a shiver and febrile disturbance pointed to an acute infective process. Further, the paresis of the right internal rectus, and the nystagmus indicated that the ravages of the virus, whatever its nature were widespread and not limited to the spinal cord. The pyrexia, at the time when the patient was examined/

examined by the writer, was accounted for by an acute cystitis.

A PERIPHERAL TYPE characterised by SYMPTOMS indicative of POLYNEURITIS.

Mrs W. aged 32, was seen upon March 23rd, 1919.

The patient who lived in an isolated farm house in the country, stated that her illness commenced during the last week in March. According to her medical attendant, she had been feverish and had complained of headache for a few days. There was no history of influenza or of sore throat. The patient was a total abstainer. About the same time the patient first noticed what she described as a 'prickly feeling' in the hands and feet which had been gradually progressive and had extended up the limbs as far as the hips. This was accompanied by increasing weakness in the lower limbs. There had been no difficulty in passing water. About March 13th, she had to take to bed because of the weakness in the legs and had remained in bed since.

When examined upon March 23rd, a slight degree of weakness of both lower limbs was detected, while in addition, there was some ataxia associated with a slight loss of the sense of position in the lower limbs. The paresis was symmetrical and no one group of muscles was affected more than another. The knee and ankle jerks were absent and the plantar reflexes were of the flexor type. No sensory loss was detected. The patient complained of some tingling in the hands, but no weakness or definite sensory loss was observed in the upper extremities apart from astereognosis in both hands. There was no calf tenderness. There was no facial weakness or immobility. There was no strabismus nor obvious defect of the ocular muscles although definite nystagmus was observed on lateral deviation and particularly in the right eye on looking to the left. The pupils were rather large in size, equal, and reacted well to light. No evidence of disease was detected in the other organs of the body. The/

The Wassermann reaction on the blood serum was negative.

REMARKS. The symptoms presented by this patient pointed to a polyneuritis, anomalous features being the febrile onset, the presence of ataxia, the absence of marked weakness of the lower limbs, the diplopia and nystagmus.

MORBID ANATOMY.

Permission for a post-mortem examination was obtained in only one case. For a report on the histological findings in this case, the writer is indebted to Dr. James Miller, who has also made a series of bacteriological observations upon several of the cases included in the series.

I. MACROSCOPIC ANATOMY.

Surprisingly little change is visible to the naked eye in the brain of individuals who die from this disease.

In the case above referred to in which the writer had an opportunity of examining the brain after death, the following abnormal appearances were noted.

- (a) A slight degree of congestion and oedema of the brain, in particular of the grey matter, more especially in the region of the mid brain and pons.

(b)/

(b) A slight but definite degree of distension of the ventricular system.

(c) Punctiform areas, notably in the pons and thalamic region, which looked like small haemorrhages, but which were proved by subsequent microscopic examination to be dilated blood vessels.

No changes were noted in the membranes of the brain, nor were any definite haemorrhages observed.

MARINESCO, the distinguished Professor of Neurology in Bucharest, has described in detail the anatomical changes observed in two cases of encephalitis, recently submitted to him for examination at the Maudsley Institute. He reports as follows:-⁽⁵²⁾

"An inspection with the aid of a hand lens already gave fairly precise information in the topography and distribution of the military haemorrhages and of the haemorrhagic stippling situated in the neighbourhood of the floor of the fourth ventricle, in the formatio reticularis and in the grey matter of the Sylvian aqueduct, the locus coeruleus, the substantia nigra Soemmeringi, etc. Further, one could even recognise with a hand lens a greyish shading around the hyperaemic vessels, which corresponded probably with inflammatory infiltration. In the cerebellum, neither in the grey/

"grey matter nor in the white, could one detect
 "the haemorrhagic stippling, and very seldom striae
 "of hyperaemia. The cerebral cortex was equally
 "unaffected, nevertheless I discovered some puncti-
 form haemorrhages in a limited region of the sphe-
 "noidal lobe and in the basal ganglia".

Dr. JAMES MCINTOSH, in a report on mate-
 rial obtained in 40 cases collected for the Local
 Government Board, says:-
 (52)

"Many of the cases showed some congestion of the
 "brain, increase of cerebrospinal fluid, with a dila-
 "tation of the vessels of the pons and the thalamic
 "region. No actual haemorrhages were seen in any of
 "the material I examined, but the dilatation of the
 "vessels was, in many instances, likely to be mistaken
 "for haemorrhages. Examination by means of a hand
 "lens, definitely showed, however, that these haemorr-
 "hagic-looking areas were in reality dilated blood ves-
 "sels. Two superficial haemorrhages were recorded,
 "one a small one, on the cortical surface, and the
 "other of some considerable size in the cerebellar re-
 "gion. In one or two cases the grey matter was more
 "prominent than usual, while in others again, it was
 "yellowish in colour."

At the post mortem on the case already re-
 ferred to, a broncho-pneumonia, probably a terminal
 infection, was met with. A similar condition was not-
 ed/

ENCEPHALITIS LETHARGICA.
(Case VI., page 68)

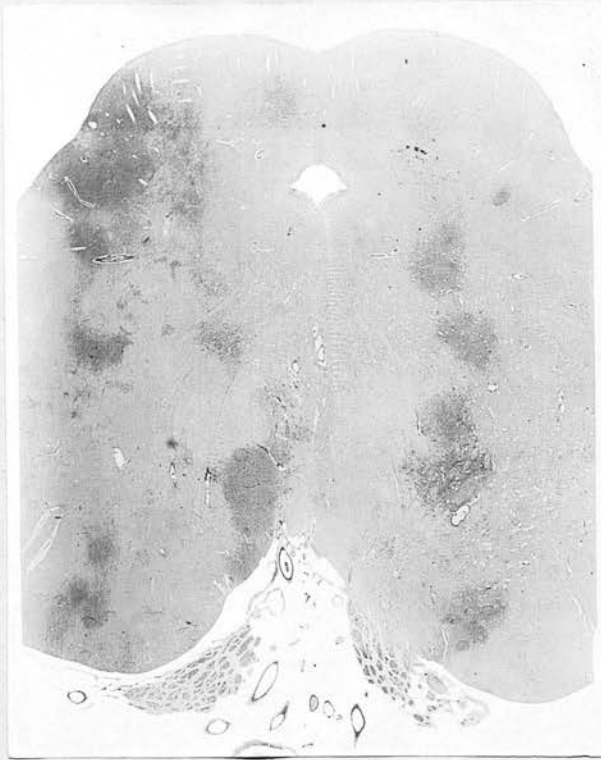


Fig. 1. Section through mesencephalon showing a number of dilated vessels.

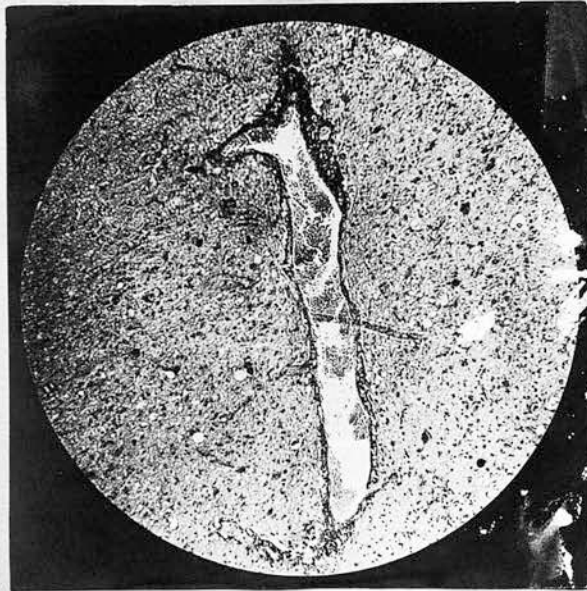


Fig. 2. A dilated vessel in the mesencephalic region showing the perivascular infiltration.

noted in some of the cases collected by the Local Government Board.

HISTOLOGY. The writer's thanks are due to Dr. James Miller for kind permission to publish a note of the Histological findings in two cases of encephalitis lethargica which he has examined. The clinical features presented by one of these cases have already been referred to (CASE VI.).

"A complete investigation was made in each instance including brain and spinal cord".

"As regards the changes in the organs other than the central nervous system, CASE I. showed a well marked purulent bronchitis and early broncho-pneumonia with the usual toxic changes in heart, liver, kidney and spleen. CASE II. showed marked congestion of the lungs with oedema, some purulent bronchitis but no consolidation of the lung. The toxic changes were less marked than in CASE I. The appearances were, in short, those which one is accustomed to find in cases of influenza of the type at present met with.

"Microscopic changes in the central nervous system. The changes varied in intensity in different parts and, without going into detail, it may be stated generally that they were most marked in the grey matter of the pons. In CASE II. there were marked changes also in the grey matter of the spinal cord the medulla appearing to be relatively unaffected./

ENCEPHALITIS LETHARGICA.
(Case VI., page 68).

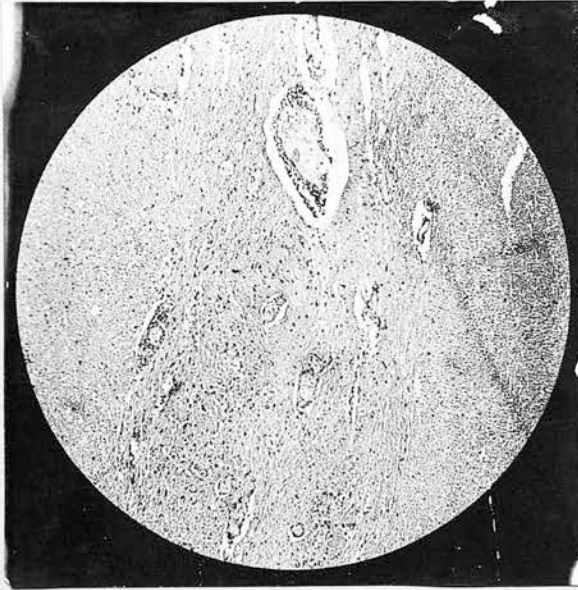


Fig.3. Dilated vessels in the posterior horn of the spinal cord showing pronounced perivascular infiltration.

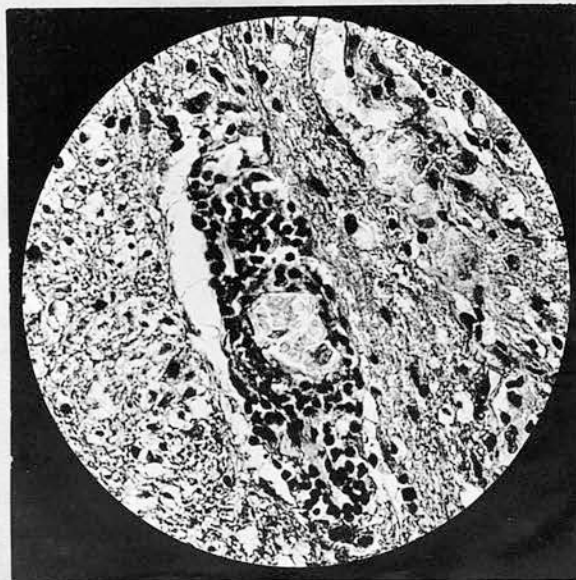


Fig.4. One of the vessels from the same section.

"unaffected. The chief changes were as follows:-

- " 1. Congestion of vessels which are distended
" with blood and stand out prominently under
" the low power.
- " 2. The presence around these vessels of nume-
" rous small round cells which may be called
" lymphocyte-like cells, there being very
" little protoplasm and the nucleus being
" round and staining deeply with haematin
" and the blue of Leishman's stain.
- " 3. Areas of pigmentation evidently represent-
" ing old haemorrhages. The pigment was am-
" orphous and was contained within phagocy-
" tic cells.
- " 4. Cellular infiltration of certain collections
" of ganglion cells notably the third nucle-
" us in CASE II., the cells being proliferat-
" ed neuroglia cells and lymphocyte-like
" cells."
- " 5. Chromatolytic changes in the ganglion cells
" specially affected, i.e. those of the pons.
" The nuclei show pale staining and a ten-
" dency to margination. The Nissl spindles
" show progressive destruction.
- " 6. Oedema of the cerebral tissue indicated by
" a/

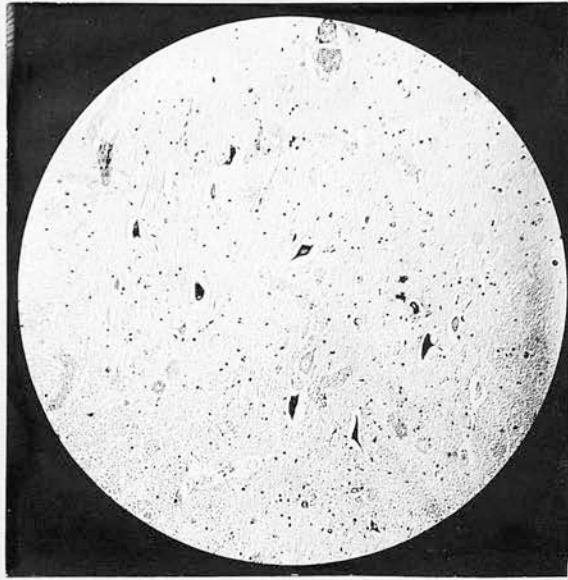


Fig.5. Nerve cells in the anterior horn
of the spinal cord.

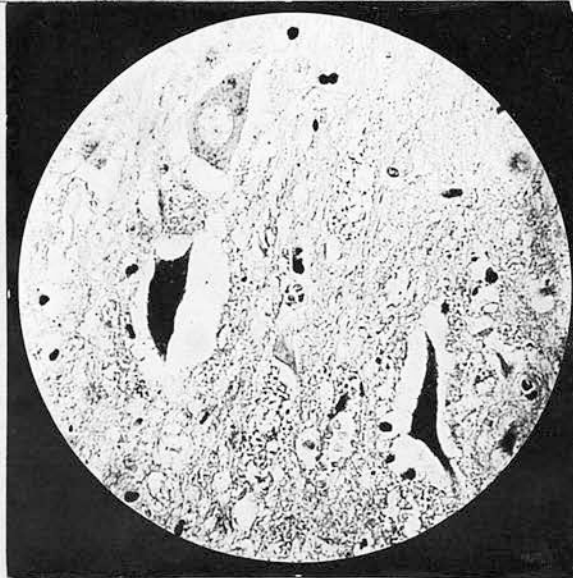


Fig.6. Some of the cells from the same
section.

N.B. The photographs are by Mr. Richard Muir
from sections prepared by Dr. James
Miller.

" a distended perivascular lymph space and
 " by large spaces scattered through the
 " white matter.

" In these two cases there were no very re-
 "cent haemorrhages although in a case examined by me
 "at the Royal Infirmary these were strikingly present.
 "No organisms were present so far as I could see.
 "Mitotic figures described by MARINESCO were not pre-
 "sent.

" The microscopic changes are thus of a sub-
 "acute inflammatory nature associated with destruc-
 "tion of the ganglion cells and a tendency to haemorr-
 "hage. The distribution of the changes varies some-
 "what in different cases, but shows a special incidence
 "in the pontine nuclei. The changes can also be ob-
 "served in the cord".

The Local Government Board obtained mate-
 rial from twenty cases for their investigation.
 The following summary of the histological appearances
 is based chiefly on Dr. JAMES MCINTOSH's observations
 upon this material and in particular upon the record
 of two cases examined by Professor MARINESCO. (52)

DISTRIBUTION of the LESIONS. The membranes
 were but slightly involved, the lesion usually con-
 sisting/

consisting of a degree of hyperaemia with some increase of cells around the blood vessels. The lesions were most noticeable and most extensive in the basal ganglia, upper part of the pons, grey matter of the floor of the fourth ventricle, much less prominent in the medulla, and very slight or absent in the spinal cord.

CHARACTER of the LESIONS. The abnormal appearances essentially consist in pronounced dilatation of the blood vessels in the affected area together with a cellular infiltration of the perivascular lymphatic sheaths, more especially of the small and medium-sized veins, and a cellular infiltration of the parenchyma.

The perivascular infiltration may be very dense, although the cells may sometimes be seen to be distinctly separated from one another as if there were oedema present. The cells are chiefly lymphocytes which show small mononuclear varieties. Polinuclear leucocytes are comparatively rare.

The parenchymatous or extra-adventitial infiltration is usually diffuse and generally varies with the degree of perivascular change; the cellular exudate, too, is very similar to that seen around the vessels, consisting in part, apparently of/

of lymphocyte cells, in part of proliferated neuroglia. The presence of giant cells with abundant protoplasm is noted by MARINESCO. Foci of infiltration are occasionally to be observed, while small microscopic haemorrhages are sometimes to be seen in close proximity to a small vessel. These haemorrhages may be from 2 to 5 times the size of the lumen, and no obvious necrosis of the vessel wall was observed by MARINESCO in relation to them.

The ganglion cells are not much involved, though some of the cells in especially affected areas may be seen to be globular in shape their chromatin being diffuse, and it may be one or more mononuclear cells lying in their close proximity. Neuronophagia is rare.

BACTERIOLOGY.

As has been mentioned, within three days of the appearance of the papers by WILFRID HARRIS and ARTHUR J. HALL, the Medical Research Committee, acting in cooperation with the Local Government Board, made arrangements for a complete bacteriological investigation, and Dr. JAMES McINTOSH of the London Hospital Laboratory undertook the bacteriological examination of some of the cases, pathological material/

material, and suspected articles of food, from the point of view of a possible relationship of botulism to the epidemic. It is unnecessary here to refer to the details of this elaborate investigation, suffice it to say that "all findings were negative as regards the possibility of the bacillus botulinus having anything to do with the epidemic. * * *

"Bacteriological evidence may be said to completely rule out the question of the bacillus botulinus playing an etiological rôle in these cases of encephalitis".

VON WIESNER (quoted by MARINESCO) who investigated ECONOMO'S cases believed he had succeeded in transmitting the disease to a macacus rhesus monkey, and affirmed that he had cultivated a gram positive diplostreptococcus from the central nervous system of subjects dying from encephalitis lethargica. These observations have not, however, been confirmed.

MARINESCO states that he has met with appearances in some of the nerve cells in encephalitis lethargica, which had all the appearances of diplococci and "were taken to be such by the majority of the bacteriologists who examined my specimens. Morphologically they were identical with diplococci, which appeared to be surrounded by an aureole resembling a capsule. But one fact which inclined me to be/

"be cautious in my final judgment as to the microbic nature of these corpuscles was that the cells containing them had no nuclei and therefore the possibility of their being chromosomes occurred to me".

McINTOSH'S results are summarized as follows:-

" From none of the post-mortem material was the pleomorphic coccus, described by ROSENOW, in poliomyelitis cases, isolated. The blood taken by venipuncture was in each instance sterile and where microbes were demonstrated with certainty, in the cerebrospinal fluid, subsequent examination proved that there was an error in diagnosis. Cultures of the nasopharynx failed to demonstrate the constant presence of any particular organism or even of a particular type. Similarly samples of faeces gave nothing from which any conclusion could be arrived at except that one found no evidence of the bacillus botulinus."

Dr. JAMES MILLER, who has investigated five of the writer's cases of encephalitis lethargica, has kindly furnished him with the following report:-

"Five cases of the disease have been examined as fully as possible as regards the bacterial flora.

" CEREbroSPINAL FLUID. In the four cases in which the/

" the Cerebrospinal Fluid was examined bacteriologi-
 " cally a diphtheria-like bacillus was isolated. All
 " were Neisser-positive in some degree. All showed
 " acid production in Hiss' glucose serum.

" SPUTUM. In three of the cases similar organisms
 " were isolated from the sputum. They resembled the
 " germs from the Cerebrospinal Fluid morphologically
 " and culturally. In the other case no sputum was
 " obtainable. The diphtheroid bacilli were present
 " in large numbers in the films of the sputum and an
 " examination of a series of specimens of sputum
 " taken at random from cases in the hospital showed
 " only occasional diphtheroid bacilli in small num-
 " bers.

" It is not contended that these organisms are
 " causally related to the disease. At present the
 " only statement that can be made is, that they do
 " not appear to be contaminations and that they do
 " not occur so constantly in cases other than enceph-
 " alitis.

" NASOPHARYNGEAL SECRETION. This was examined
 " in all five cases. Meningococcus-like organisms
 " were present in four of the cases. In two the
 " strains agglutinated with Gordon's type sera; one
 " case being Type II., the other Type III.

" FAECES/

" FAECES. In one of the cases a non-lactose
 " fermenting organism was isolated which agglutinat-
 " ed with Flexner's serum to a fairly high dilution.

" WASSERMANN. In all cases both serum and
 " cerebrospinal fluid gave a negative result.

" WIDAL. Two cases having been inoculated
 " gave the usual results with B.T.: B.P.A. and B.P.
 " B. one of the cases gave agglutination in an un-
 " usually high dilution with B.P.B.

" PHARYNGEAL SWABS. Cultures on blood se-
 " rum shewed diphtheroid bacilli in larger or small-
 " er numbers in two cases.

" The results of animal inoculations with
 " strain of diphtheroids isolated cannot at present
 " be given in full.

" EXPERIMENTAL. The only experimental ob-
 " servations as yet reported in the literature
 " with the exception of ECONOMO'S investigations
 " (the writer has been unable to obtain ECONOMO'S
 " original papers) are those of McINTOSH. (52) The
 " latter author's statements regarding his inocu-
 " lation experiments may be quoted in full:-

" The failure to demonstrate the
" presence of a particular micro-organism
" and the poliomyelitis character of the
" cellular infiltration in a nervous tissue
" suggested that experimental inoculations
" of the ^{pathological} ~~bacteriological~~ material might throw
" some light on the disease. Accordingly
" material from eight of the fatal cases
" was injected into macacus rhesus monkeys.
" The inoculations consisted of emulsions
" of pieces of the basal ganglia, pons,
" medulla and cervical cord, and in one case,
" pieces of the cord were used alone. The in-
" ^{oculations} ~~oculations~~ were all done intracerebrally,
" while an intraperitoneal

" intraperitoneal injection was given simultaneously.
 " The emulsion of the nervous tissue was prepared by
 " pounding the tissue in a glass mortar with normal
 " saline; of this 0.5 to 1.0 c.c. was injected into
 " the frontal lobe after trephining in the middle line
 " just above the supraorbital region, and as a rule
 " 5 to 10 c.c. was injected into the peritoneal cavity".

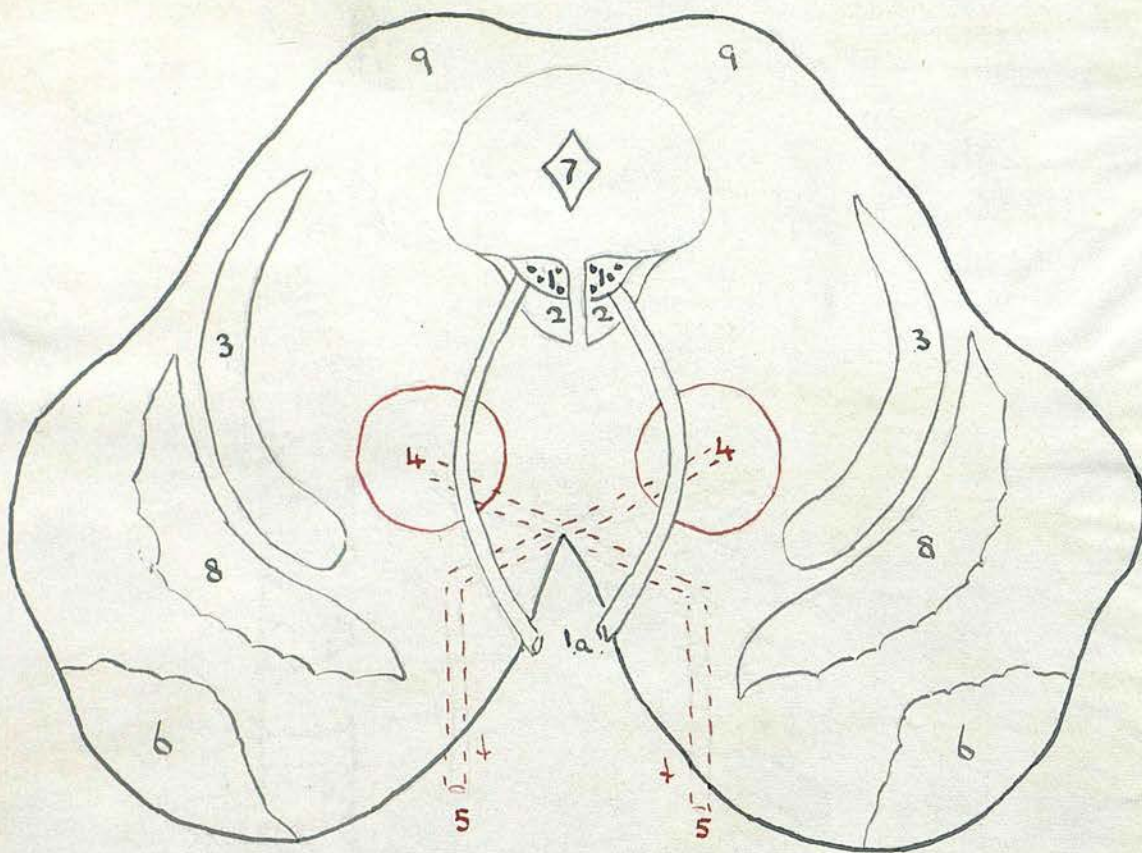
" In no case did any definite paralysis develop
 " even after an interval which could be regarded as
 " the longest average incubation period. One monkey
 " however, became paralysed 84 days after the inoculation.
 " There was a definite flaccid paralysis
 " of the legs in no way differing from that observed
 " in experimental poliomyelitis. But no characteristic
 " inflammatory changes were found in the central
 " nervous system. The condition arose from changes occurring
 " outside the nervous system, and an account of
 " the actual findings, which are not without special
 " interest, will be reported elsewhere. One or two
 " of the cases, however, some ten days after the inoculation,
 " showed some slight excitement and tremblings,
 " as is occasionally noticed before the onset
 " of experimental poliomyelitis. This was only noticed
 " for a day or two and then passed off, the
 " animals regaining their usual vigour.

" The material used for inoculation was preserved
 " for/

" for three or four days before the inoculation in
 " 50% glycerine; this strength of glycerine is
 " known not to affect the virus of poliomyelitis.
 " It might be suggested, however, that ^{as} in encephali-
 " tis lethargica the disease runs a more protracted
 " course than does poliomyelitis, the virus may
 " have completely disappeared from the system by
 " the time the patient dies. This is probably true
 " in a certain number of the cases, but is not true of
 " all, as material was obtained from two or three
 " cases which died from the 7th to the 9th day of
 " the disease..

" To date there is no record in the literature
 " of the successful inoculation of material from
 " cases of encephalitis, even taken during an epide-
 " mic of poliomyelitis, while the intracerebral ino-
 " culation of poliomyelitis virus practically always
 " produces a spinal disease."

" In this instance the negative results indi-
 " cate that the virus is not exactly the same as
 " that of poliomyelitis for 1912, when Dr. Turnbull
 " and myself working under identical conditions, suc-
 " ceeded in inoculating several monkeys with polio-
 " myelitis virus obtained from different cases which
 " had died in the London Hospital".



Diagrammatic representation of a section through the mesencephalon illustrating the gross relationship of some of the structures referred to in the text implication of which affords an explanation of certain symptoms presented by cases of encephalitis lethargica.

1. The Third nerve Nucleus with the third nerve (1 a) arising from it..

2. The Posterior Longitudinal Bundle.

3. The Mesial Fillet or great afferent thalamic tract..

4. The Red Nucleus..

5. The ~~Red~~rospinal Tract.

6. The ~~Afferent~~ Corticospinal or Pyramidal Tract.

7. The Iter or Aqueduct of Sylvius..

8. The Substantia Nigra..

9. The Anterior Corpora Quadrigemina.

INTERPRETATION of the SYMPTOMATOLOGY.

A study of the morbid anatomy throws some light upon the symptomatology of encephalitis lethargica.

The febrile disturbance is explained by the inflammatory nature of the lesion, while the distribution and anatomical features of the latter account for the frequently bilateral and usually incomplete character of the pareses, together with the fact that, as a rule, these eventually subside without leaving any permanent effects.

The paresis of the oculo motor, of the facial and, it may be, of other cranial nerves, is obviously due to implication of their respective nuclei.

Nystagmus, which is so frequent, ^{may be} is accounted for by interference with the posterior longitudinal bundle.

The mask-like face, the attitude so reminiscent of paralysis agitans and the rhythmic tremor indistinguishable from that observed in Parkinson's disease, all of which symptoms are met with in occasional cases, are no doubt to be explained by interference with the function of the red nucleus or rubrospinal tract.

The/

The cerebellar ataxia observed in one type of encephalitis lethargica is accounted for by implication of the cerebellar peduncles. All the symptoms above mentioned are consequently directly referable to disease affecting the tegmentum of the mesencephalon and pons.

The general asthenia and occasional absence of the knee-jerks are no doubt due to involvement of the motor nuclei in the spinal cord and, it may be, to changes in the peripheral nerves to which the pains in the limbs sometimes complained of, are ^{prob-}ably ~~ob-~~viously referable.

In exceptional cases in which Babinski's sign is observed, sometimes in association with exaggerated knee-jerks, the efferent cortico spinal tracts are obviously affected.

The mode of production of the lethargic state is less obvious. The facts that headache and vomiting when they occur are transient symptoms, that optic neuritis is not met with and that the cerebrospinal fluid is not under tension justify the assertion that the state of lethargy is not dependent upon a general increase of intracranial pressure, a conclusion which is corroborated by post-mortem evidence. Again, a study of the literature appears to show that generalised oedema of the brain is not a pronounced feature in these cases. This being so, the/

the question arises whether the lethargic state may not be explained by the focal lesion in the mesencephalon and brain stem. As is well-known, the optic thalamus constitutes a receptive centre for all afferent stimuli, and the view has been advocated by MACNALLY that the lethargic state is due to an interruption of the afferent stimuli passing to the thalamus. This suggestion, it may be noted, is not original, since it was advanced many years ago to account for the lethargy in the condition described as "NONA". The writer is inclined to accept this as perhaps the most reasonable explanation of the facts. The circumstance that in sleeping sickness and basal syphilis, pronounced morbid drowsiness is respectively a constant and frequent symptom is suggestive, in the writer's opinion, in this connection. It must be admitted, however, that in other disorders in which there is no evidence of an anatomical lesion in the brain stem, a stuporose state apparently indistinguishable from the lethargic state and due either to a toxoemia or to a general increase of intracranial pressure may be observed.

The/

THE PLACE of ENCEPHALITIS LETHARGICA as a
SYMPTOM COMPLEX.

Encephalitis lethargica, it has been affirmed, constitutes a clinical entity. In the differentiation of such an entity, it is necessary to formulate distinctive features to which all cases must conform before they can, with justice, be included. The selected cases which constitute the basis of the foregoing description, present a symptomatology so similar that they may, without hesitation, be regarded as conforming to an entity which is characterised by the lethargic state, by febrile disturbance and by pareses of certain cranial nerves, notably the third and seventh pairs. It is true that in some of these cases, one, in some another, of the symptomatic triad was either inconspicuous/

inconspicuous or even absent, but in all the association of symptoms was such as to leave no doubt as to their dependence upon the same morbid process.

Errors of two kinds may arise in the description of a new symptom complex. On the one hand, the confines of the group may be too rigidly drawn, while on the other, characteristics which are affirmed to be distinctive, may be too indefinite, with the result that cases of a different nature may be included. Prior to the detection of a common etiological factor or the discovery of a specific pathological agent, it is probably wise to limit the scope of the symptom complex, emphasising characteristic features which are beyond dispute, rather than attempting to include within the bounds of the new entity cases which, although presenting very suggestive points of resemblance, cannot, in view of their somewhat different symptomatology, be clearly proved to be of a similar nature. This is the method which has been adopted in the present thesis.

Again, there is a danger that, in attempting to differentiate a symptom complex, when no single symptom is absolutely pathognomonic, undue weight may, perhaps, be attached to one symptomatic feature. Thus, as has been mentioned, a condition indistinguishable from the lethargic state is met with/

with occasionally in a variety of other conditions. Again, in discussing the symptomatology, it has been noted that in some cases of encephalitis lethargica, the lethargic state occupies an altogether subsidiary place in the clinical picture.

If the lethargic state is eventually proved to be due to focal changes in the brain, subsequent observations may demonstrate that encephalitis lethargica is not to be regarded as a disease, but that the term is merely applicable to a group of symptoms dependent on a pathological process which shows a special predilection for the region of the mesencephalon and pons but which may affect other parts of the central or peripheral nervous system. For the present, however, it certainly appears advisable to retain the nomenclature advocated by ECONOMO, until the Pathologist differentiates the organism responsible for the disease and evolves some intravital method of demonstrating the nature of the infection. Until this is so, the confines of the clinical picture can only be enlarged, as has been indicated, by the recognition of cases which/

which while presenting the clinical features of the new symptom complex, also present manifestations obviously dependent upon involvement of other parts of the nervous system.

FACT and SPECULATION bearing on the
NATURE of ENCEPHALITIS LETHARGICA.

Certain facts may be laid down before the field of speculation is entered upon.

In the first place the case records embodied in this thesis demonstrate, it is submitted beyond doubt, the existence of a symptom complex which presents definite and distinctive features. Again the writer's previous experience and the statements of those observers who have contributed to the meagre literature upon the subject justify the conclusion that this symptom complex is of recent incidence. Further, anatomical evidence has proved that the symptoms are dependent upon an Encephalitis. Lastly, although the symptomatology and morbid anatomy of Encephalitis Lethargica clearly indicate the infective nature of the process and its almost certain organismal origin, the Bacteriologist has not, as yet, been able to demonstrate with certainty, the specific cause, and Laboratory methods have hitherto proved of no aid to the Clinician except in a negative/

negative sense.

The available data consequently permit of the conclusion that Encephalitis Lethargica is a definite clinical entity of recent origin which is dependent upon an infective process, the causative virus of which is still unknown.

These are the submitted facts. Subsequent considerations are of necessity of a more or less speculative character.

A variety of problems present themselves, among others the following:-

Is the new symptom complex to be regarded as a disease which is dependent upon a specific agent? If so, is that agent something which has only recently made its appearance in the organism? May it be that the agent in question is one which has been lying dormant and only been roused into activity by predisposing circumstances which were not present in the past? On the other hand, is it possible that the symptoms may be attributable to the modification of a virus brought about in one way or another, the virus having hitherto produced symptoms of a different kind? Again, is it the case that the virus of Encephalitis Lethargica has a selective action upon the mesencephalic region of the brain and, if so, can any explanation be advanced to account for this?

In/

In attempting to answer these various questions, the only available existing data are those derived from analogy.

The very definite and constant clinical picture presented by typical cases of Encephalitis Lethargica indicates beyond a doubt that the process is one which affects notably, though not necessarily exclusively, the mesencephalon. Further - anatomical observations also demonstrate, that although changes may be observed throughout the central nervous system, both brain and spinal cord, it is essentially the mid brain and pons which are the seats of the most pronounced lesions. These facts, for such they are, warrant the conclusion, either that the virus is possessed of special selective qualities or that the mesencephalon is, for some reason or another, especially predisposed to attack. Since the nature of the virus is undetermined and since experimental evidence has hitherto been of a negative kind, possible information bearing on this point can only be expected by a comparison with other known affections which are of a similar though different nature and which resemble encephalitis lethargica in their clinical, pathological or epidemiological features. Two affections call for special consideration in this connection/

connection, viz:- Botulism and Acute Poliomyelitis. Botulism resembles encephalitis lethargica in that the nervous symptoms are very similar, the pathological process affecting the same region of the brain, while Poliomyelitis, like encephalitis lethargica, is an infective process dependent on a virus which appears to have a selective action.

BOTULISM.

BOTULISM. The term Botulism was coined in Southern Germany towards the beginning of the nineteenth century and applied to a peculiar type of food poisoning which was caused by the ingestion of spoiled sausages. At a later date, it was proved that the same symptom complex might also be produced by poisoning from other articles of food, for example, smoked meat, fish and tinned beans, and that it might also be closely simulated by poisoning from cheese. Numerous outbreaks have been reported throughout Germany, where the condition has been recognised for more than a century. Several outbreaks have also been reported in America.

VAN ERMENGEM in 1895 isolated an organism now known as the bacillus botulinus, and proved that in botulism the poisoning is due to a toxin which/

which is produced when the bacillus is grown upon suitable media.

The resemblance which the symptoms of botulism present to those of Encephalitis Lethargica are obvious, when one compares a summarised conclusion arrived at by ERMENGEM in 1897. Referring to the symptomatology of Botulism, this author, quoted by ERNEST C. DICKSON, says:-

"The Botulism syndrome consists essentially of
 " a collection of neuro-paralytic phenomena; dis-
 " turbances of secretion of the ^mprinæ viae and sym-
 " metrical motor paralysses complete or partial de-
 " pending in all probability upon lesions of the
 " pons of the medulla, but chiefly of the nuclei
 " of origin of various cranial nerves and of the
 " anterior horns of the spinal cord.

" It is characterised:-

" (1) By arrest of secretion or a hyper-
 " secretion of saliva and of the
 " buccopharyngeal mucus.

" (2) By external and internal ophthal-
 " moplegia more or less complete,
 " (ptosis, mydriasis, paralysis of
 " accommodation, diplopia, internal
 " strabismus).

" (3) By dysphagia, aphonia, obstinate
 " constipation/

- " constipation and retention of
 " urine.
 " (4) By a general feebleness of con-
 " traction in all the voluntary
 " muscles.
 " (5) By the absence of pyrexia, of dis-
 " turbance of general sensibility
 " and of the intelligence.
 " (6) To these phenomena are often added
 " disturbances of respiration and of
 " the circulation which may lead to
 " death, more or less rapid as a con-
 " sequence of bulbar paralysis.
 " (7) Finally, the characteristic mani-
 " festations make their appearance at
 " most from 12 to 24 hours after the
 " ingestion of the poisoned food.
 " They are often preceded by tempo-
 " rary gastro-intestinal symptoms.
 " They appear gradually and they per-
 " sist for several weeks."

A comparison of the symptomatology of Botulism, as depicted by ERMENGEN with the foregoing description of Encephalitis Lethargica shows that the two affections have many points of resemblance, while further in both the lesion is situated in/

in the mid brain.

On the other hand, certain facts clearly demonstrate that Encephalitis Lethargica is quite distinct from Botulism. For instance, in the latter disease, there is no febrile disturbance, and drowsiness it appears, is not a prominent symptom. Again cases of Encephalitis Lethargica do not occur in groups but appear sporadically throughout the country, nor is there a history of food poisoning. Important evidence is also available from the standpoint of morbid anatomy for MARINESCO⁽⁵²⁾, who years ago made an elaborate study of material derived from Van ERMENGEM's cases of Botulism and who has recently studied the histological appearances in encephalitis lethargica, is definitely of opinion that the former is not a true inflammatory process and that the lesions met with, although they affect the same portion of the brain, are distinct from those observed in the latter affection.

Lastly, and most important of all, the bacillus botulinus which is discovered apparently with the greatest ease in cases of Botulism has not been demonstrated in encephalitis lethargica.

Botulism and encephalitis lethargica are thus, two perfectly distinct conditions which, although/

although presenting ^{some} similar clinical features are obviously due to different causative agents both of which tend to affect the same portion of the nervous system.

ACUTE POLIOMYELITIS resembles Encephalitis Lethargica in certain of its features, and it has been suggested that the latter disease may be due to a modification of the same virus which is responsible for the former.

The two affections resemble each other, in that both are dependent upon an infective process and in that both the causative agent attacks the central nervous system. Further the sporadic manner in which cases of both these disorders crop up throughout the country is very similar.

Points of difference would, however, appear to be opposed to the view that the resemblance is more than superficial. In support of this assertion, the following arguments may be advanced:-

1. POLIOMYELITIS is a disease which has long been recognised, whereas Encephalitis Lethargica is a new disease and not merely one which in the past has failed to attract attention.

2./

2. Some years ago when acute poliomyelitis was comparatively frequent throughout the country, no cases of Encephalitis Lethargica were observed by the writer. Again, during the past year, there has been no increased prevalence of poliomyelitis.
3. The writer has not met with a single case of Encephalitis Lethargica in which local spinal symptoms, similar to those met with in poliomyelitis, were observed.
4. With the exception of the two cases reported in the literature and already referred to (p. 32) no instances of direct infection have been recorded. It must be admitted in this connection that for long poliomyelitis was regarded as a sporadic affection and that it is only in comparatively recent times that cases of infection by contagion have been observed.
5. The age incidence is different. The great majority of those who suffer from acute poliomyelitis are children or young adults. The writer, it is true, has met with one case of acute poliomyelitis in a man of 48. (Dr. F. E. BATTEN who also saw this case had no doubt as to its nature), but he has observed/

observed no other case in which the patient was attacked after the age of 30. On the other hand, Encephalitis Lethargica would appear to be an affection more especially of later life. It is true that BATTEN and Still have described under the term 'Epidemic Stupor' a condition met with in infants, which is very similar to, if not identical with, encephalitis lethargica but Dr. J. S. FOWLER informs the writer, that as far as he knows, no cases of this kind have been observed, either in the Children's Hospital, or in the neighbourhood of Edinburgh.

6. The seasonal incidence would appear to be different. Acute poliomyelitis occurs much more frequently in the late summer and autumn, whereas the writer's observations suggest that encephalitis lethargica is especially prone to occur during the colder months of the year.
7. Although the mode of onset with febrile disturbance and stupor may be very similar in the two conditions, premonitory symptoms extending, it may be over a period of two or three weeks are often observed in encephalitis lethargica, while in acute poliomyelitis this is not the case.

8. Pronounced meningeal symptoms, notably neck rigidity and Kernig's sign, are frequent though far from universal at the onset of poliomyelitis.
9. Drowsiness which may be present for a few days during the febrile stage of an acute poliomyelitis never persists for weeks or even months, as is the rule in encephalitis lethargica.
10. The encephalitis which is observed in association with epidemic poliomyelitis, does not appear to select any special region of the brain, while bulbar cases, as WICKMAN and others have pointed out, are of rare occurrence.
11. The temperature in acute poliomyelitis usually persists for only two or three days to a week, whereas in encephalitis lethargica some febrile disturbance may persist as the writer has demonstrated, for two or three weeks.
12. Although the symptoms of encephalitis lethargica may be very protracted, the writer's experience suggests that, as a rule, they clear up entirely, whereas, in the great majority of cases of poliomyelitis, some permanent/

permanent paralysis persists.

13. Although the histological lesions in both conditions are of much the same type McINTOSH states, that a close examination brings out many minor points of difference.

14. Experience has shown that acute poliomyelitis may be readily produced in animals inoculated from tissues derived from a case of this nature. Hitherto all attempts to produce encephalitis lethargica by a technique precisely similar in detail have completely failed.

While it must be admitted that encephalitis lethargica and acute poliomyelitis present certain points of resemblance, the facts do not appear to warrant the assumption of an intimate relationship and are not in themselves sufficient in view of the many points of difference between the two affections, to justify the conclusion that the two disorders are dependent upon a modification of the same organism, although they do not completely negative this possibility.

INFLUENZA has been very prevalent all the world over during the past year, and the possibility of a relationship of some kind between encephalitis lethargica and this disease naturally arises./

arises. It is indeed surprising to find no reference to influenza in the Report of the Local Government Board and particularly since so long ago as 1890, cases of encephalitis associated with influenza were reported by LEICHTENSTERN⁽⁸⁾ and several other observers. In 1893 NAUWERCK⁽¹²⁾ cultivated the influenza bacillus from a case of encephalitis, while CANTANI proved in 1896, that an encephalitis may be produced experimentally, by injection of dead cultures of the influenza bacillus. OPPENHEIM⁽¹⁶⁾ and SOUTHARD⁽¹⁷⁾ indeed, both recognise an influenzal encephalitis and SOUTHARD'S statements with reference to the symptomatology, may be quoted.

" If there is anything which distinguishes
 " this form of encephalitis, it is a gradually in-
 " creasing loss of consciousness, taking several
 " hours or a day for its completion. The patient
 " can, as a rule, be roused by sharp stimuli, and the
 " pupillary reflexes are normal. The projection sys-
 " tem is not characteristically involved at the on-
 " set. Meningitic symptoms, such as stiffness of
 " neck and opisthotonos, are exceptional. There is
 " irregularity in the temperature, which is rarely
 " high until the cerebral symptoms are well under-
 " weigh. Some of the febrile temperatures are, per-
 " haps, due to intercurrent infections (OPPENHEIM).
 " But these statements were made before the question
 " of/

" of influenzal septicaemia had engaged attention.
 " The pulse is likely to be slow at first, but before
 " death quicker, small, and irregular.

" The focal symptoms develop, as a rule,
 " after coma has set in, not apoplectically, but one
 " by one (STADELMANN'S case with onset suggesting
 " cerebral haemorrhage is a rare exception). More-
 " over, in a limb about to become paralysed, there
 " are often premonitory symptoms, such as weakness,
 " numbness, or convulsions. Sometimes the convul-
 " sions involve the whole side of the body, when the
 " eventual loss of power is to be a monoplegia. The
 " paralyzes may be quite masked by coma, or a diffe-
 " rence in the two sides may be detected by chorei-
 " form movements on one side only. The variety of
 " onset and course is so great, that LEICHTENSTERN⁽⁸⁾
 " felt that there are limiting cases in which a hemi-
 " plegia may develop without coma on a truly influ-
 " enzal basis. Almost every possible focal symptom
 " has been described in cases of encephalitis deve-
 " loping after influenza; but motor symptoms far
 " outnumber sensory ones".

The symptomatology of influenzal encephali-
 tis as depicted by SOUTHARD does not resemble that
 of encephalitis lethargica. OPPENHEIM, however,
 remarks that headache, vertigo, nausea or vomiting,
 apathy/
^{closely}
⁽¹⁶⁾

apathy, drowsiness and general weakness are premonitory symptoms of influenzal encephalitis and may be hard to interpret since they are apt to be regarded as merely incidents in convalescence from ordinary influenza. A careful study of OPPENHEIM'S work on encephalitis seems to clearly show that the focal nervous symptoms of the reported and personally observed cases, upon which he bases his clinical description, were much more varied and the site of maximum intensity of the lesion in consequence, not so constant as is the case in the symptom complex referred to in this thesis. Admitting that influenza may produce an encephalitis, though in the past the recognised symptomatology has not been so constant as to permit of a diagnosis from the character of the focal nervous symptoms, the question arises, may not the symptom complex referred to as encephalitis lethargica, be of influenzal origin? The suggestion is an attractive one and the writer confesses that he expected to find evidence in support of this view. In only three of the series of 20 cases which were specially selected for analytical purposes was there, however, a history of an immediately preceding attack of influenza and as already mentioned, in none of these was the available evidence absolutely conclusive. In the great majority of cases there was no/

no history of symptoms indicative of a recognised influenzal infection at the time of onset. Two other patients, it should be mentioned, had complained of nasal catarrh a week or two before the onset of the encephalitis, while in two additional cases, recently observed, the patient had undoubtedly had an influenza immediately prior to the encephalitis. Since such a large proportion of the population had been recently affected with influenza, it seems scarcely permissible to draw any further deduction from these facts ^{that} ~~than~~ the preceding illness may have predisposed to the subsequent infection. That influenza has a pronounced influence in predisposing to disease or in lighting up disease already in existence, is a well-recognised fact. Reference to disseminated sclerosis is of interest in this connection. About the time that influenza became so prevalent, a number of neurologists reported their experience as to the relative increase in frequency of cases of this disease, and the suggestion was even made that disseminated sclerosis might be due to an influenzal infection. That cases of disseminated sclerosis did become more frequent about this time and that this was not an apparent increase due to advance in diagnosis, is the opinion still held by many observers of experience.

The/

The writer, who for some time paid special attention to this point, satisfied himself that in the great majority of cases of disseminated sclerosis in which the first symptoms were said to have appeared as a sequel to influenza, careful enquiry elicited the fact that inconspicuous symptoms clearly indicating the presence of the disease prior to the attack of influenza, were in existence. It may be, indeed, that an influenzal infection, although it does not in itself produce an encephalitis, predisposes to the action of an organism which is lying latent in the tissues.

FINALLY: The facts that the causative agents of botulism and of WERNICKE's superior encephalitis, the former of which is undoubtedly, while the latter is in all probability, quite distinct from that of lethargic encephalitis, affect the same region of the brain, would appear to the writer to suggest rather a predisposition to attack on the part of this special region, than a selective action on the part of the virus.

DIAGNOSIS Again, the writer is inclined to think that there is some relationship between an influenzal infection and encephalitis lethargica, but he submits that the available data rather favour the/

the view that the influenzal infection does not,
in itself, produce the encephalitis, but that
certain types of influenzal infection ^{may} predispose
to the action of a specific organism which is
lying latent in the tissues.

DIAGNOSIS/

D I A G N O S I S .

Diagnosis is always difficult when a disease presents no constant characteristic feature, when it varies greatly in its clinical manifestations, when there is no evidence of a common etiological factor, when cases occur sporadically, when the exact pathological cause is undetermined and when the laboratory can give no help by isolating the causative agent.

Under such circumstances, a diagnosis can only be arrived at -

FIRSTLY by a consideration of the symptoms and signs which the individual case presents, its mode of onset and its course and

SECONDLY by the exclusion of other disorders which may simulate it.

The latter process - recognition by exclusion - plays indeed, at the present time a prominent rôle in the diagnosis of encephalitis lethargica. Clinical acumen and judgment, together with the physician's general experience of disease, are consequently often called into play to an exceptional degree, & they may be severely taxed in arriving at a conclusion in some of the cases with which/

which he meets. Two groups of cases, each of which presents a variety of types, have been referred to in a previous chapter. The first of these, which may be stigmatised as the mesencephalic group, is characterised by focal symptoms, which are to be explained by a lesion in the mid brain, implicating the afferent sensory paths proceeding to the optic thalamus, and it may be the third and seventh nerve nuclei, the rubrospinal tract, the cerebellar system, and possibly, other adjacent structures, while the second group includes cases in which an infective process of unknown origin has selected the cerebrum, the spinal cord or the peripheral nerves, as the site of its activities. Reasons have been adduced - notably the facts that the anomalous cases included in the latter group have only been observed recently, and that the ocular muscles are liable to be involved, unlike cases of polyneuritis and acute myelitis observed by the writer in the past, for believing that ^{latter} these cases may, very possibly be due to the same virus which produces encephalitis, lethargica. In discussing the problem of diagnosis, however, it is not proposed to consider this second group, the relation of which to encephalitis lethargica is still undetermined.

A typical case of encephalitis lethargica which is characterised by the lethargic state, pyrexia and focal nervous symptoms, notably ocular and facial palsies - cannot well be mistaken for any other disorder by one who has previously met with cases of a like nature. On the other hand, with the exception of the lethargy which cannot be regarded as pathognomonic, no single manifestation is, in itself in any way characteristic or distinctive.

Errors in diagnosis may be of two kinds, FIRSTLY inexcusable or rather avoidable errors in which the disease is not recognised because the practitioner is not conversant with its symptomatology, or it may be with unusual features which an individual case presents and -

SECONDLY unavoidable or excusable errors in which the present state of knowledge does not permit of a dogmatic opinion upon the data available in any given instance.

There can be no doubt that encephalitis lethargica is not at present, generally recognised by medical men throughout the country. Among the thirty cases or so, in which the writer made a definite diagnosis, in only three had the condition been previously suspected. Again and again he has been asked by
able/

able practitioners to see cases of the kind which puzzled them, since the cases in question did not conform with clinical pictures with which they were familiar, or of which they had read. The explanation would appear to be that beyond three or four papers and some brief reports in the 'Lancet' and Proceedings of the Royal Society of Medicine, there is practically no literature upon the subject, while, further, during the war, the busy practitioner has probably not had time to read his journals.

The disorders which encephalitis lethargica may closely simulate and the actual difficulties in diagnosis which consequently arise are numerous.

A variety of premonitory symptoms which, as has been indicated, may occur during the prodromal stages, are apt to prove misleading. Thus such symptoms as defective vision, diplopia, giddiness and pain in a limb, were among those complained of in cases examined by the writer. At this period, however, the available data are probably no more than suggestive, if indeed they arouse suspicion.

The disorders for which encephalitis lethargica may be mistaken fall into three groups.

- I. Conditions characterised by such general symptoms as drowsiness, stupor, and it may be/

be delirium, accompanied in certain instances by headache, vomiting and febrile disturbance, e.g. meningitis, (meningococcal and tuberculous) typhoid fever, influenza, pneumonia, apoplexy, internal pachymeningitis, uraemia, diabetic coma, cerebral syphilis, cerebral arteriosclerosis, acute alcoholism and general states of debility and exhaustion.

- II. Conditions characterised by focal nervous symptoms which may be progressive, e.g., intracranial tumour, myasthenia gravis, paralysis agitans and disseminated sclerosis.

III. Hysteria and other neuroses.

Those affections which are most likely to give rise to difficulty in diagnosis, call for individual consideration.

1. INFLUENZA. During the past year influenza has been rife throughout the country and it is only to be expected that cases of a little known symptom complex, such as encephalitis lethargica, which are characterised by febrile disturbance and it may be inconspicuous focal manifestations, should often be erroneously regarded as examples of the prevalent malady. Although evidence has been adduced which seems to demonstrate that an encephalitis may be determined by the influenza virus, the cases of encephalitis recently met with have seldom been preceded by typical symptoms of an influenzal infection. Indeed, in only three of the writer's series/

series of cases was there a history of immediately preceding influenza, and in not one of these was the proof conclusive. Consequently, the absence of headache, pain in the limbs and catarrhal symptoms in any given case, favours the view that the fever and lethargic state are due to the virus of encephalitis lethargica and not to that of influenza.

When focal symptoms indicative of a lesion in the brain stem are met with, in addition to the general manifestations, proof as to the existence of a mesencephalic encephalitis is practically conclusive.

2. CEREBROSPINAL FEVER was diagnosed in three cases of the present series. In none of these cases, however, was the difficulty a very real one. Pronounced rigidity of the neck and hamstring muscles, enlargement of the spleen and a pronounced leucocytosis are seldom, if ever met with, in encephalitis lethargica, while persistent severe headache and high temperature & herpes labialis (although noted in one of the writer's cases of encephalitis), and the chorioid are very rarely observed in this disease. A lumbar puncture will afford conclusive evidence, should further corroboration be required, for in cerebrospinal meningitis, the fluid is under pressure, it is almost invariably turbid or purulent and the meningococcus is detected on microscopical examination/

examination or cultivated, if the correct technique is adopted.

3. TUBERCULOUS MENINGITIS appeared to be a possible explanation of the symptoms in one case, in which there was a suspicious history to the effect that the patient had suffered from tuberculous disease of the spine in early life. The circumstance that the subject of encephalitis is usually in good health, and has not been losing weight prior to the onset of his illness, the absence of evidence of tubercle elsewhere, and in this connection tubercle of the choroid deserves special mention, and the facts that there is rarely any neck rigidity or a pronounced Kernig sign in encephalitis when considered in relation to the positive symptoms present, should rarely leave the diagnosis in doubt. Here, again, a lumbar puncture may prove of service for the cerebrospinal fluid in encephalitis lethargica is quite clear, is not under pressure and rarely contains any excess of cellular elements.

4. A possible relationship between acute POLIO-MYELITIS or POLIOENCEPHALITIS has been suggested. This question has been discussed, suffice it to say this problem in differential diagnosis has not hitherto arisen in the writer's experience. It must be admitted/

admitted, however, that the febrile disturbance, headache and vomiting and the state of drowsiness observed at the onset of some cases of poliomyelitis, might give rise to difficulty. The fact, that in the early stages of acute poliomyelitis, there is a pronounced excess of cells in the fluid withdrawn by lumbar puncture, may prove to be of value in differentiating the two conditions.

5. APOPLEXY. This was the diagnosis suggested in two or three cases seen by the writer, but in each instance the possibility was dismissed with certainty when the facts were elicited. In this connection, the presence or absence of valvular disease of the heart, of thickening of the peripheral vessels, of a high blood pressure, and of albumen in the urine, are of importance. When syphilis is suspected, the Wassermann reaction is to be tested both in the blood and cerebrospinal fluid. Needless to say an encephalitis might well occur in an individual who happened at the same time to be the subject of cardiovascular disease or syphilis. The character of the focal symptoms of encephalitis lethargica together with the absence of symptoms referable to any particular arterial distribution, are points of essential moment in the solution of this problem in differential diagnosis, should it arise.

6. PACHYMEMINGITIS HAEMORRHAGICA. Drowsiness which varies in degree from time to time is a prominent feature in internal haemorrhagic pachymeningitis. As a rule, a history of chronic alcoholism, evidence pointing to the existence of general paralysis, of senile dementia, or some disease of the blood, all of which conditions may predispose to this affection, is forthcoming. The writer has observed two or three cases, however, in which an internal haemorrhagic pachymeningitis occurred in the absence of any such predisposing cause. The diagnosis, where this is so, may be extremely difficult. (49) It is possible, indeed, as FARQUHAR BUZZARD has pointed out, that a haemorrhage on the internal surface of the dura mater may be associated with an encephalitis.

7. TYPHOID FEVER was a possibility which arose in two cases, in one of which, not included in the series selected for analytical purposes, there was no doubt that the patient actually had an attack of enteric fever, while the writer is satisfied in addition, that there was an associated encephalitis of the mesencephalic type. Difficulty is apt to arise in those cases of encephalitis lethargica, in which the local nervous symptoms are inconspicuous/

inconspicuous or possibly even absent. Among other positive symptoms which may serve to differentiate enteric fever are abdominal distension, discomfort and tenderness, diarrhoea, the typhoid rash, the special features of the temperature curve, and enlargement of the spleen. The Widal reaction in doubtful cases may clinch the diagnosis.

8. PNEUMONIA. Although the writer had personally met with no case of encephalitis lethargica in which this question in diagnosis had arisen, SAN/⁽¹⁴⁾TOIN asserts that this constitutes a problem which is apt to give rise to difficulty. The points of distinction are obvious.

9. URAEMIA may undoubtedly give rise to a symptom complex simulating encephalitis lethargica. This was so in one case, but further examination permitted of the definite exclusion of this condition. The examination of the urine, of the cardiovascular system and of the optic discs should place the diagnosis beyond doubt.

10. DIABETIC COMA was the diagnosis advanced in one case, on the grounds that the urine contained sugar and acetone. This suggestion, in the case in question, did not, however, afford an adequate explanation of the ptosis, changes in the reflexes etc.,/

etc., which were present. The exclusion of diabetes in this case was justified by the fact that repeated examination of the urine failed to corroborate the original observation as to the presence of sugar and acetone.

11. ACUTE ALCOHOLISM. When describing the symptoms of a typical case, the close resemblance between encephalitis lethargica and the appearances presented by a patient suffering from acute alcoholism, ^{was} ~~were~~ referred to. The resemblance is, however, a superficial one, which is not likely to give rise to any real difficulty on further examination.

12. CEREBRAL ARTERIOSCLEROSIS. Drowsiness and slow mental action associated it may be with some degree of emotional instability are common accompaniments of arteriosclerosis of the cerebral vessels. The vascular accidents which are apt to occur in this condition may give rise to a variety of local nervous manifestations. A history of gradual mental failure, and it may be of previous cerebral attacks, together with evidence of arterial disease, are points to which attention is specially to be directed.

13. The resemblance between the symptoms of encephalitis and those of BOTULISM has been referred to./

to. Botulism as has been mentioned, is almost unknown in this country. Cases of Botulism occur in groups. The diagnosis depends upon the recognition of a causative dietetic factor and the demonstration of the *Bacillus Botulinus*, which is apparently easily detected in the stools.

14. The physiognomy of PARALYSIS AGITANS may be closely simulated by encephalitis lethargica. An immobile expressionless face, although there may be no demonstrable weakness in the facial movements, and a rhythmic tremor indistinguishable ^{from} to that which is characteristic of Parkinson's disease may be observed in the latter disease. Notwithstanding the resemblance in the general appearance which is sometimes presented, there can be little real difficulty in distinguishing between the two affections, for in Paralysis Agitans the onset is gradual while lethargy and paresis of the ocular muscles are not observed in this disease.

15. INTRACRANIAL TUMOUR may constitute a very real difficulty in diagnosis, especially when there is no definite history of early somnolence and febrile disturbance. Tumours in the region of the mesencephalon and pons may produce ocular palsies similar to those observed in encephalitis lethargica while, as is well known, new growths in this situation/

situation are often unaccompanied by symptoms of increased intracranial pressure (headache, vomiting, and optic neuritis). Further, in some cases of encephalitis lethargica, the focal symptoms indicate clearly that the local lesion is progressive. Two cases, in both of which the writer believed the lesion to have been an encephalitis, illustrate the difficulty in diagnosis which may arise. It has been suggested by NONNE, that in some of the reported cases in which an intracranial tumour is said to have become latent, the actual lesion was probably an encephalitis and not a tumour. A case of this kind, which was brought before the Edinburgh Medico-Chirurgical Society by Dr. JOHN THOMSON, many years ago, and which was demonstrated by the writer at a Meeting of the Society comparatively recently, is an illustration in point. It is almost unnecessary to remind the reader that the first symptoms exhibited in a case of intracranial tumour are sometimes directly referable to a haemorrhage into the growth. In cases such as this, a diagnosis can often only be arrived at by a process of exclusion. Gliomata, as is well known, are of not uncommon occurrence in the region of the mid brain and pons, assuming in the latter situation/

situation an appearance which has given rise to the term pseudo hypertrophy of the pons which is sometimes applied to these neoplasms. These tumours infiltrate the substance of this portion of the brain and for long the nervous tissues may be spaced and their function remain intact. The occurrence of localised haemorrhages or foci of degeneration in the growth may account for the only symptoms which the case presents. As can be readily understood, the differential diagnosis in a case of the kind may conceivably be one of great difficulty.

16. DISSEMINATED SCLEROSIS. On one occasion the differential diagnosis from disseminated sclerosis was by no means easy. The patient, a girl of 20, was taken somewhat suddenly ill with diplopia, vertigo and vomiting; the vertigo was intense, so much so that the patient dared not lift her head from the pillow, in case the movement should intensify the symptom and bring on an attack of vomiting. Drowsiness had not been a conspicuous feature. On examination, however, marked nystagmus was elicited, the knee jerks were somewhat brisk, and the abdominal reflexes absent, while there was a bilateral extensor response. Further, it was ascertained that a year previously she had consulted Dr. Traquair, on account of some defect of vision, which she described as "seeing double". Now, the symptoms of disseminated sclerosis/

sclerosis occasionally come on as suddenly as in this case, while the history of diplopia almost a year previously suggested that the pathological process responsible for the symptoms had very possibly been in existence for a considerable period. It was subsequently ascertained, however, that the defect of vision was merely related to a high degree of myopia, and that at the time the patient consulted Dr. Traquair, there was no evidence of paresis of the ocular muscles. A striking instance, in which disseminated sclerosis made its appearance in a very similar manner to the onset in the case above described, was that of a young man who was under the care of Dr. Hughlings Jackson at the time the writer was a house-physician at the National Hospital. Intense vertigo accompanied by vomiting when any attempt was made to lift the head from the pillow, in association with other symptoms indicated the existence of a unilateral lesion affecting the cerebellar system, very probably a tumour of the brain. It was decided to operate, but after the patient had been removed to the surgical wards of the hospital, further observation suggested that it would be wise to postpone operative interference. This delay was justified, since the symptoms eventually in large part passed off. A year later, however, this patient was re-admitted/

readmitted to the same hospital with the typical symptoms of disseminated sclerosis. He died of an intercurrent affection, and at the post mortem the clinical diagnosis was confirmed, while an old patch of sclerosis was detected in the middle peduncle of the cerebellum on one side, this lesion having evidently been responsible for the early symptoms manifested by the patient.

To return to the case originally referred to a careful consideration of all the facts, in particular the rarity of such an onset in disseminated sclerosis and the presence of headache, the probabilities undoubtedly seemed to point to encephalitis lethargica, a diagnosis which was confirmed by the subsequent progress of the case.

(16)

17. MYASTHENIA GRAVIS. OPPENHEIM and CASSIRER in their Monograph on Encephalitis discuss at some length, the differential diagnosis between this condition and myasthenia gravis. This is ~~not~~ a problem which has never presented itself to the writer in a practical form. Bilateral facial paralysis, ptosis and asymmetrical ocular palsies certainly occur in myasthenia gravis as common symptoms, and in cases of encephalitis lethargica in which there is no very definite history of an acute febrile onset, of drowsiness/

drowsiness or stupor, the possibility of error might arise. The subject of encephalitis lethargica not only looks, but actually is, drowsy, while the patient with myasthenia gravis is, as a rule, perfectly alert.

18. FUNCTIONAL NERVOUS STATES. Attention has been drawn by some authorities to the fact that emotional disturbance is frequently observed in association with the symptoms of the disease at present under discussion, although such symptoms were only noted in two cases of the present series. In the absence of any signs of febrile disturbance or of any certain distinctive indications of an organic process, the error of diagnosing encephalitis lethargica as a neurosis can be understood. In one case in which the writer made this mistake, the temperature, which was normal at the time he examined the patient, rose two days later and the patient died, evidently from encephalitis lethargica within a week.

PROGNOSIS .

Five of the cases in the present series (25%) terminated fatally.

Two of these cases were typical instances of the disease, in which pronounced lethargy, febrile disturbance and ocular palsies occurred in association. Two patients showed profound lethargy with some degree of febrile disturbance, but no pronounced focal signs. The fifth case was one in which, as previously mentioned, a diagnosis of probable hysteria was advanced, but which ultimately developed symptoms indicating its true nature.

The ages of the patients who died were as follows:-

24, 27, 45, 47 and 60.

The duration of the illness, it is interesting to note, was almost the same in each instance, the shortest period being eighteen, the longest twenty-two, days after the appearance of the first symptom. In this connection it may be mentioned that the average duration of the illness in the twenty-five fatal cases collected by the Local Government Board was twenty-one days, the shortest/

shortest being six, the longest forty-nine.

The writer's experience does not justify him in formulating any very definite conclusions in relation to prognosis; it would seem, however, that if the patient survives the first three weeks of the illness, the strong probabilities are that he will recover. Pronounced stupor, dysphagia and loss of sphincter control are symptoms of serious moment though not necessarily indicative of a fatal termination.

The rate of recovery is usually very slow. The patient may remain in much the same condition for weeks or even months (in one severe case the patient's condition remained practically in statu quo for three months after his admission to hospital); on the other hand, in abortive cases, recovery may be complete after two or three weeks. In some cases the lethargy passes off after two or three weeks while focal symptoms remain.

Recovery was eventually complete in the majority of the cases here reported; in others, however, certain symptoms still persist, and it is as yet too early to express an opinion as to the ultimate result in these cases.

T R E A T M E N T .

No therapeutic measures have been so far proved to have a definitely beneficial effect upon cases of encephalitis lethargica. A specific therapy has yet to be discovered.

Hexamin in doses of ten grains, four-hourly may be given in the early stages in the hope that this drug, which is known to be excreted into the cerebrospinal fluid, may prove of service by its antiseptic action. Flexner's observations, it may be recalled, suggest that urotropin retards, and may even arrest, the development of experimental poliomyelitis in the monkey. This procedure was employed in all the cases seen within a few days of the onset of the illness, but in no single instance were any clinical observations made which clearly indicated that the drug had proved to be of undoubted benefit.

Obstinate constipation is very usual in the early stages of the disease and the use of calomel and other purgatives has been advocated for its relief. In one or two instances the writer was informed that the lethargy was less pronounced as a result of this treatment. Since the lethargic state may depend upon an oedema of the brain, it is conceivable that a hydragogue cathartic might prove effective/

effective in the treatment of this symptom.

Two cases which were under the writer's care for a period of several weeks afforded opportunities for observing the effects of remedies. The superficial resemblance between encephalitis lethargica, on the one hand and sleeping sickness, on the other, both as regards the state of lethargy and the perivascular infiltration in the brain, and the fact that arsenic possibly in the case of the former, iodides certainly in the case of the latter, are effective, suggested the use of these remedies in encephalitis lethargica. Potassium iodide, which was exhibited in increasing doses, over a considerable period, up to ninety grains in the twenty-four hours, appeared to be ineffective, as did arsenic, administered in the form of Fowler's solution, up to thirty minims in the day.

Strychnine, given hypodermically, in increasing doses up to a twelfth of a grain in the day, seemed to be of benefit in one case.

It is unnecessary in a communication such as this to refer to general therapeutic measures dictated by common sense and experience.

CONCLUSIONS.

Encephalitis Lethargica is a convenient nomenclature applicable to a group of cases which have been prevalent during the past year in this and other countries. These cases are characterised by initial febrile disturbance which is usually slight, by a state of lethargy or somnolence and by focal nervous symptoms, among which paresis of the muscles supplied by the oculo-motor nerves and of the face, are those most commonly observed. A general asthenia, associated it may be with tremor, is the rule. The cerebrospinal fluid which is not under pressure contains but little, if any, increase of cells, while the blood may show a very slight leucocytosis. A variety of clinical types ^{are} is met with:-

- (a) Typical cases in which both general and focal symptoms are pronounced.
- (b) Cases in which the lethargic state is a prominent feature, but in which focal nervous symptoms are inconspicuous.
- (c) Cases characterised by pronounced focal nervous symptoms, the lethargy being so slight that it may escape detection.
- (d) Cases in which cerebellar ataxia constitutes a striking symptom.
- (e) Cases resembling paralysis agitans.
- (f) Abortive cases characterised, it may be, by focal or general symptoms or by both, the/

the symptoms passing off in the course of two or three weeks.

In addition to the group of cases above described, an unusual number of cases of cerebral encephalitis have been observed during the past year, as also anomalous cases of ~~poly~~neuritis and myelitis. The incidence of these cases and the fact that they present symptoms suggestive of a widespread toxic agent, the nature of which is unknown, suggest that they may be due to the same virus.

The onset may be sudden, the patient falling down in an unconscious or semi-conscious state, but in the majority of cases it is insidious and is preceded by premonitory symptoms, such as defective vision, diplopia, giddiness, peripheral pains, etc.

The etiology is obscure. The sexes are equally liable and individuals of all ages may be affected. Neither occupation nor social position appear to predispose. Those affected are usually in good health when attacked, although exceptionally there is a history of preceding influenza. The available facts suggest that there is a tendency for the disease to occur during the colder months of the year. With two exceptions, no instances have been reported in which there has been a history of infection/

infection or contagion. Syphilis and alcohol play no etiological role.

On post-mortem examination the only visible change is, as a rule, some dilatation of the blood vessels notably in the region of the mesencephalon and pons. Haemorrhages may, however, be observed. Upon microscopic examination dilatation of the blood vessels with a perivascular lymphocytic infiltration most pronounced in the mesencephalic region, although it may be met with in other parts of the brain and in the spinal cord, is a constant feature.

The focal nervous symptoms are to be explained both as regards their localisation and character by the features of the lesion. Thus, the ocular and facial palsies are accounted for by involvement of the respective nerve nuclei, the nystagmus by implication of the posterior longitudinal bundle. The cerebellar ataxia and the mask-like face and rhythmic tremor so suggestive of paralysis agitans, which are met with in some cases, may be explained by implication of the cerebellar peduncles and of the rubrospinal tract respectively, while the asthenia is accounted for by involvement of the motor cells and of the grey matter of the spinal cord. The explanation of the lethargic state is not/

not definitely determined. It may be either a focal symptom due to interference with afferent impulses passing through the mesencephalon to the optic thalamus, while on the other hand it is impossible to deny that it may depend upon a more widespread change, possibly an oedema, throughout the brain.

No definite organism has, as yet, been discovered to which the symptoms can be attributed.

Dr. James Miller's observations on the presence of a Neisser positive diphtheroid bacillus in the cerebrospinal fluid are of much interest, but animal experiments are necessary before any further statement can be made regarding a possible causal relationship between this organism and encephalitis lethargica. Isolated observations suggest a path of ingress by way of the throat or nose. Botulism is in no way related to encephalitis lethargica. Although the anatomical appearances, the clinical symptoms and the epidemiology of encephalitis lethargica present resemblances to acute poliomyelitis, the points of difference preponderate. The available facts suggest that while the two conditions are probably allied, they are not due to the same virus. A possible relationship to influenza is suggested by the simultaneous incidence of this disease within the/

the past year, and the view is advanced that influenza may predispose to encephalitis by lowering the resisting power and thus facilitating the action of a specific organism. The available data rather favour a predisposition on the part of the mesencephalon than a selective action of the virus.

A great variety of clinical conditions simulate or are simulated by encephalitis lethargica. Among these may be mentioned meningitis, influenza, enteric fever, pneumonia, uraemia, alcoholism, apoplexy, the superior polioencephalitis of WERNICKE, epidemic poliomyelitis, botulism, intracranial tumour and hysteria.

The prognostic data are uncertain. Five patients in the present series (25%) died. The majority eventually recover although it may be several months before recovery is complete. In a minority of cases it is affirmed that some degree of mental weakness, ocular palsies, or some degree of general weakness persist.

No treatment is known which has any certain effect.

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A CHRONOLOGICAL ABSTRACT of LITERATURE on
 ENCEPHALITIS with SPECIAL REFERENCE to
 ENCEPHALITIS LETHARGICA.

18. LONGUET. Semaine Médicale 1892 (quoted by WILSON)
 reviews the literature upon a mysterious
 disease referred to as "Nona" which occurred
 in epidemic form in Italy and Hungary during
 the spring of 1890. These were cases of
 encephalitis and they were characterised by
 stupor, lethargy, and catatonia. The
 contention was advanced that the cause of
 the pathological sleep frequently noted in
 "Nona" was due to the incidence of the lesion
 in the grey
 matter of the iter and anterior part of
 the floor of the fourth ventricle.
19. VON ECONOMO. Verein f. Psych. u. Neurol. in
Wien, April 17th 1917
Wien Klin. Wochenschrift, May
10th, N. 30. S. 581. 1917
Neurologisches Centralblatt.
Nov. 1st 1917.
 In April 1917, this author reported the
 presence in Vienna of cases which close-
 ly correspond with those here reported.
 He introduced the name encephalitis
 lethargica.

20. VON WIESNER, Wien.Klin.Wochenschrift, July 26,1917,
(quoted by MCINTOSH Local Government Board
Report p.61) who examined ECONOMO'S cases,
"claims to have isolated a diplococcus which
on inoculation into monkeys produced a hae-
morrhagic encephalitis **but no** histological
changes suggestive of those seen in the
cases from which the material was derived".
21. MATTHEWSON. Med.Journ. of Australia, Oct.27,1917
(quoted by BASSOE, Nervous & Mental Diseases
Vol.VIII, p.81 1918) had under his care at
Brisbane Children's Hospital seventeen pa-
tients, eleven of whom had been suffering
from a disease characterised by a sudden or
insidious onset. High temperature, convul-
sions, headache, vomiting, stupor, and un-
consciousness were symptoms observed in some
of these cases. The bacteriological examin-
ation of the cerebrospinal fluid proved ne-
gative, while a widespread congestion of
the blood vessels of the brain and spinal
cord and an infiltration in their adventiti-
al sheath with large and small mononuclear
cells, including plasma cells were observed
in the one case which was examined histolo-
gically.

22. BREINL. Med. Journ. of Australia, Mar. 16, 1918, records nine cases in which the clinical symptoms resemble those in the cases recently reported in this country, and reviews no less than seven papers upon the same subject which had been published in the same Journal during 1917. The patients were for the most part children. They showed for a few days previously headache and other signs of malaise, or they were suddenly attacked by convulsions and a high fever and soon after passed into coma. Neither Babinski's nor Kernig's sign was constant; the knee-jerks were exaggerated, head-retraction was marked in some cases but absent in others. Nystagmus was present now and again. Several patients had tremors of the arms and legs, while others had frequent and violent convulsions, and several showed opisthotonos. Intestinal disturbances were not uncommon. Lumbar puncture yielded a clear fluid, not under increased pressure, which showed but a slight increase of cells. Seven cases were examined post mortem, the changes present being indicative/

indicative of an encephalitis, while four showed lesions typical of acute poliomyelitis in the cord. BREINL contends that the disease is a form of poliomyelitis, and his cases are certainly in many respects dissimilar to those described in this thesis. The Reviewer is inclined to think that these cases are more likely to be instances of poliomyelitis than of the affection under consideration.

23. NETTER. Soc.Méd.des Hôp.de Paris. Mar 22, 1918.
Bull. de l'Acad. de Méd. Mar.22, April 12,
 19,26., May 3, 7, 1918.

records an outbreak in Paris and its immediate neighbourhood of similar cases to those under discussion. A number of case reports and brief reports of discussions appeared in the transactions of the Medical Societies of Paris, notably the Société Médicale des Hôpitaux. NETTER, who took part in nearly all these discussions is of opinion that Encephalite Lethargique epidémique is not a form of poliomyelitis.

24. WILFRED HARRIS. Lancet, Apl.20, 1918, under the term "Acute Infective Ophthalmoplegia or Botulism" refers to seven cases met with by him in the course of a fortnight. HARRIS sums up the symptomatology of his cases as follows:-/

follows:-

"The striking features common to all the cases have been the acute onset of double third nerve paralysis, incomplete, with bilateral ptosis and diplopia, and well marked drowsiness. Pyrexia has been present in the majority and retention of urine in five cases. Obstinate constipation has been present in all, and delirium in four of the cases being very active and resembling delirium tremens in two cases. The optic discs have been normal in all, and the cerebrospinal fluid also has shown nothing abnormal, except an excess of lymphocytes in one case".

In one of HARRIS' cases, Captain Harrison, R.A.M.C., succeeded in growing an organism from the stools and urine which in its features resembled closely the morphological characteristics of *Bacillus Botulinus*, although "cultures had not been obtained at the time this paper was written in order to prove its identity by experimental inoculation".

25. HALL, ARTHUR J., Lancet, Apl.20, 1918, reports that he had recently met with ten cases unlike anything he had previously observed. HALL summarises the main characteristics of the cases so far observed as follows:-

"The patient whilst in ordinary health begins to be languid and drowsy, with or without headache and other symptoms of malaise/

" malaise. In a few hours or days the weakness
" has increased very much, and indeed may am-
" ount to complete prostration, so that he lies
" helpless in bed and can hardly move a muscle.
" Together with this, the drowsiness becomes
" more marked and develops into real lethargy.
" Pyrexia may be absent throughout or it may
" be present from the first, becomes severe and
" persists. Cerebral excitement and delirium
" have been prominent features in some of the
" cases. In most of them local symptoms point-
" ing to lesions in the bulbopontine area are
" present sometime or other, of these ptosis,
" ophthalmoplegia of various extent, nystagmus,
" facial palsy of lower neuron type, unilateral
" or bi-lateral, speech affections and dyspha-
" gia have occurred in different combinations
" in different cases. Muscular tremors of a
" curious kind have been observed in some; in
" one case this formed the most prominent symp-
" tom, and alcoholism was suspected. In some
" cases the general muscular asthenia has been
" more marked on one side of the body than on
" the other, - either arm alone or leg; but
" there has been as yet, no evidence of a lo-
" calised limb paralysis such as one commonly
" sees/

" sees in acute poliomyelitis".

This author recognises two types, a meningitic and an asthenic type, according to the character of the symptoms. The facial appearance in the case of one woman was so suggestive of 'Parkinson's mask' that HALL actually, at first thought she had this disease. The posture of the hands, too, resembled that assumed in paralysis agitans, although the tremor had no resemblance to the tremor of that disease. Hall expresses no opinion as to the nature of the affection.

26. MCFADDEN, A.W.J., Lancet Apl.27, 1918. In a letter under the title of "Botulism" MCFADDEN, on behalf of the Local Government Board, appeals to Medical Officers of Health, to send him full particulars as to cases of the kind, especially as regards food history.
27. DOBSON, LEONARD, Lancet Apl.27, 1918. In a letter to the Lancet this author describes a typical case under the title of "Acute Infective Ophthalmoplegia or Botulism".
28. McCAW, H.J.; J.R.PERDRAU, and F.G.STEBBING, Lancet Apl.27th, 1918, under the title "Toxic Bulbar Paralysis (possibly Botulism)" these observers, in a letter to the Lancet, report six cases/

cases all of which correspond to the meningitic type described by HALL.

29. FARQUHAR BUZZARD, Lancet, Apl.27, 1918, In a letter to the Lancet entitled "Toxic Encephalitis". This observer reports a case very similar to paralysis agitans. He says, - "it seems possible that there is a prevalent poison, whether the bacillus botulinus or some other virus, which attacks the nervous system and produces different pictures, according to its incidence on this or that part of the brain, but with a special predilection for the brain stem and mid brain region."
30. CROOKSHANK, F.G., Lancet May 4, 1918, writing under the title "Botulism?", states in a letter to the Lancet that since the third week in March, he has seen no less than twenty cases of the kind at the time being described. He points out that during the latter part of 1916, cases of "peripheral polyneuritis sometimes with unilateral facial paralysis" were occurring in the army in France, and he suggests that the possibility of a relationship between these cases and those at the time being described in this country, is worth while bearing in mind.
He/

He goes on to say that "the cases all correspond to the clinical descriptions given of acute polio-encephalitis and that we should not too hastily assume that all cases of polio-encephalitis now met with are due to B. Botulinus."

31. BROADBENT WALTER. Lancet May 4, 1918, in a letter to the Lancet describes shortly a case of encephalitis, the onset of which occurred two days after the patient had eaten tinned salmon and sausages. The bacteriological examination was quite negative.
32. BROCKBANK, E.M. of Manchester, Lancet, May 4, 1918, in a letter to the Lancet gives short notes of two cases both of which present the typical features of encephalitis lethargica "which suggest that botulism has appeared in this district".
33. BATTEN, F.E. and GEORGE F. STILL, Lancet, May 4, 1918, in a paper entitled "Epidemic Stupor in Children" refer to four cases occurring during the last week of February and first three weeks of March in which stupor developed rapidly, without convulsions. There was generalised rigidity, a cataleptic condition, rhythmic tremor/

tremor of the hands, a mask-like face, a divergent squint, and irregular nystagmoid movements of the eyes. The children did not speak. There was no neck rigidity. The children after being placed on their legs were able to walk with some encouragement. Incontinence was present. The temperature was slightly raised for a few days. The pulse was slow and there was profuse perspiration. The cerebrospinal fluid was under normal pressure and showed no cytological change. The Wassermann reaction was negative. After lying for three to five weeks in a stuporose condition, the children slowly recovered. One child stood with body bent and the arms flexed in a position resembling that adopted in paralysis agitans, his expression was fixed and there was a short shuffling gait and the retropulsion which is often seen in that disease.

34. SAINT MARTIN and LHERMITTE, Bull. de la Soc. Méd. des Hôpitaux, May 17, 1918, quoted by BASSOE, Nervous and Mental Diseases, emphasizes the diagnostic importance of the co-existence of somnolence and bilateral paralysis of the oculo motor nerves and points out that the main pathological/

pathological lesion is found in the grey matter beneath the aqueduct of Sylvius. They remark that this region has long been recognised as peculiarly vulnerable to bacterial and toxic agencies. They further, indicate that the location is the same as that in WERNICKE'S acute haemorrhagic polioencephalitis in which, however, the involvement is more extensive and the symptomatology much more complicated. These authors are not prepared to deny a relationship with poliomyelitis and they add, that an epidemic among fowls, resembling human poliomyelitis, existed at the same time in the part of France where these observations were made.

35. FARQUHAR BUZZARD, Lancet, May 18, 1918, in a letter to the Lancet, refers to two cases of acute haemorrhagic encephalitis in adults which he had verified post-mortem. The clinical picture included a rapidly progressive hemiplegia and aphasia, associated in both instances with epileptic convulsions and in one with hemianesthesia, hemianopia and optic neuritis. He remarks, - "it appears, therefore, that the inflammation may affect any part of the brain and produce a great variety of/

" of physical signs and symptoms according to
 " its incidence".

36. LORD, ROBERT E., Lancet, May 18, 1918, reports a
 probable case of lethargic encephalitis, under
 the title "Botulism".

37. CROOKSHANK, F.G., Lancet, May 18, 1918, contributes
 a paper entitled "Botulism" and Heine-Medin
 disease". This author remarks, - "on the
 " whole it may, I think, be stated with some
 " confidence, that there is at present in London,
 " and elsewhere, an outbreak of cases clinically
 " indistinguishable from examples of Heine-Medin
 " disease". He further states:- "It is possible
 " that outbreaks closely resembling those of
 " classical Heine-Medin disease or some forms of
 " that disease may be due to a virus that is to-
 " tally disparate from the virus of that disease".
 " There are, he says, "only four acute specific
 " diseases essentially affecting the grey matter
 " of the central nervous system, namely tetanus,
 " rabies, Heine-Medin disease and botulism which
 " have been shown so far, to be connected with a
 " particular virus and in all four the post-mor-
 " tem appearances may be so similar in kind that
 " for none of them can it be said they are speci-
 " fic". Later in his paper this author says:-
 "Since/

" Since these notes were written the position
" has become more clearly defined, The
" present cases it may be asserted, are
" cases of the Heine-Medin disease".

38. MELLAND, CHARLES H., Brit.Med.Journ. May 18 & 25.

1918, contributes a paper on "Epidemic Polio-encephalitis (so called Epidemic Botulism)" in which he reports thirteen cases and discusses the differential diagnosis between Botulism and polioencephalitis. The most striking difference, as he points out, lies in the fact that in botulism almost without exception, the disease occurs in groups, varying in their numbers, but including most of those who have partaken of the infected food, while in the present epidemic in no instance has any group infection occurred.

39. MARIE P. and G. TRETIAKOFF, Bull. de la Soc. Méd.

des Hôpitaux, May 24, 1918, describe the pathological appearance in two cases which had been described clinically by Chauffard and Bernard. In both cases acute inflammation had involved the brain stem, notably in the region of the locus niger and the nuclei of the oculo-motor nerves. They comment on the resemblance to the haemorrhagic superior encephalitis of WERNICKE.

40. WILSON, S.A.K., Lancet, July 6, 1918, in a paper

entitled "Epidemic Encephalitis" states that he had observed thirteen cases, seven of which two with necropsy, he reports. The cases he describes exemplify, he states, various types of the disease differing either in severity ^{or} ~~of~~ in localising symptomatology.

CASE I. Acute and fatal case with mainly mesencephalic localisation.

CASE II. Mild recovering type.

CASE/

CASE III. Ponto-medullary type.

CASE IV. Severe type with prominent mental symptoms.

CASE V. Severe and fatal case with meningeal symptoms.

CASE VI. Cortical type with lethargy, catatonia, mental symptoms.

CASE VII. Paralysis agitans type.

Among other points WILSON states that in a certain percentage of cases, meningeal symptoms, such as stiffness of the neck, pain in the neck, Kernig's sign, are present, but as a rule they are not well marked. Of the localising symptoms he states, that unquestionably the commonest grouping is of the polio-encephalitis superior type, i.e. a peri-aqueductal grouping. The cerebrospinal fluid was carefully investigated in all his cases, and in common with previous observations, the bacteriological examination was uniformly negative. In one case, the cerebrospinal fluid, showed a definite pleocytosis. Two of WILSON'S thirteen cases died; the ratio of mortality in NETTER'S cases being seven out of fifteen; and of ECONOMO'S, six out of eleven. WILSON criticises the claims of von WIESNER regarding the diplostreptococcus described by this author/

author. "It is curious there is no mention
 " of this organism in the tissues of the pati-
 " ent from whom the emulsion was made. It is
 " conceivable that the brain cord emulsion con-
 " tained some quite other specific virus and
 " that the diplostreptococcus was accidental.
 " . . other investigators have not had a simi-
 " larly successful experience". WILSON is of
 opinion that the evidence available suggests,
 "that in the present epidemic we are dealing
 " with a form of infection which has a special
 " tendency to involve the oculo-motor nuclei,
 " akin, no doubt, to the virus of poliomyelitis
 " but not identical with it." According to
 WILSON, objection may be advanced to the term
 encephalitis lethargica on the ground that it
 is illegitimate to apply a clinical adjective
 to a pathological substantive.

41. RICE OXLEY, Lancet July 6, 1918, reports a typical case.

42. CROOKSHANK, F.G., Lancet, July 13, 1918, in a letter in which he combats various conclusions, refers to points of similarity between encephalitis lethargica and poliomyelitis.

" 1. The organism found by von WIESNER in the
 " Viennese cases is, I am told by high bacteri-
 " ological/

" bacteriological authority, indistinguishable
" from ROSENOW'S diplococcus, which has been
" during the last two years so generally found
" associated with poliomyelitis in New York,
" and of which it is believed the Flexner
" bodies represent one stage. The same orga-
" nism has been identified recently in London.

" 2. Dr.BREINL concludes on the basis
" of experimental results, that the Australian
" disease and acute poliomyelitis represent
" the same affection.

" 3. WICKMAN and others have recorded
" epidemics of poliomyelitis in winter and
" spring.

" 4. LESLIE CARR has drawn special
" attention to stupor, and KOPLIK to ophthalmo-
" plegia in the New York epidemic of 1916.

" 5. In America in 1916 it was general-
" ly found that the changes in the cerebro-
" spinal fluid stood in relation with the
" "type" of case dealt with.

" 6. Of the cases that I personally
" have seen in London recently, quite a large
" proportion (perhaps 30 per cent) were "menin-
" gitic" in type in a series of over 120 that
" included/

" included seven of the "ordinary" spinal kind.
 " 7. Variations in type, - clinical,
 " epidemiological and in respect of age inci-
 " dence - are the rule and not the exception,
 " if a series of outbreaks, and epidemics of
 " poliomyelitis are considered".

The reviewer has quoted Crookshank in full although he is not of opinion that the arguments advanced by this author are by any means conclusive as to the pathological identity of encephalitis lethargica and polio-encephalitis.

43. VAIDYA, S.K., Lancet, Sept. 7th, 1918, in a paper entitled "Obscure Epidemic Encephalitis", contributes a valuable addition to the condition of the blood and cerebrospinal fluid in these cases. He reports twenty cases observed at the London Hospital. Examination of the blood showed a very small amount of leucocytosis, viz:- 8,000 to 9,000 per c.m., whereas in cases of poliomyelitis examined at the Rockefeller Institute, the count varied from 15,000 to 30,000. As regards the cerebrospinal fluid the cell count shows very small deviation from the normal and is not as grossly affected as in poliomyelitis.

(Although/

(Although the records in the individual cases are reported in tabular form no reference is made to the stage of the disease when these examinations were made, a matter possibly of very considerable importance. E.B.)

44. SAINTON, PAUL, Presse Méd. Sept. 23, 1918, in a short systematic description, describes encephalitis lethargica as a toxic, infective, epidemic syndrome characterized clinically by a triad of symptoms consisting of somnolence, palsies of the motor nerves of the eyeballs and a febrile state, and anatomically by a more or less diffuse encephalitis situated chiefly in the grey matter of the mid brain. He states that the facial nerves are frequently involved and sometimes also the motor branch of the trigeminal and hypoglossal (the reviewer has not observed paralysis of either of these nerves in the cases he has personally examined). SAINTON further notes that paralysis of the **muscles** of the neck or extremities, hemiplegia, rigidity of the neck and **back**, epileptiform attacks, ataxia, vasomotor disturbances and bed sores may occur. The cerebrospinal fluid is normal and blood cultures/

cultures negative. SAINTON is inclined to look upon lethargic encephalitis as a special variety of influenza.

45. MORAX, Brit.Journ.of Ophthal. Oct.1918, the French ophthalmologist, points out that the leading eye symptoms are ptosis, diplopia and nystagmus. Optic neuritis is not a feature of the disease. MORAX states that he has seen complete recovery in several cases, but that it is still too early to determine the average duration of the different ocular manifestations.
46. LANCET, Nov.2.1918. A Discussion on encephalitis lethargica took place at the Royal Society of Medicine upon October 22nd, the combined Sections of Medicine, Epidemiology and Pathology taking part. F.W.MOTT, who described the changes met with in two brains examined by MARINESCO, stated that the last named observer regards lethargic encephalitis as a disease entirely different from botulism, from the haemorrhagic poliomyelitis of WERNICKE, from the poliomyelitis of HEINE-MEDIN, and from sleeping sickness. MOTT, on the other hand, stated that he could find no essential difference between this epidemic encephalitis/

encephalitis and the ponto-bulbar encephalitis of OPPENHEIM and CASSIRER and the cases described by WICKMAN.

P.N.PANTON, who summarised VAIDYA'S observations on the blood and cerebrospinal fluid (vide 26), makes no statement as to the period of the disease when these examinations were carried out.

W.H. HAMER pointed out that just as in 1915, the so-called epidemic of cerebrospinal fever was really only a small part of an influenza prevalence, so in the epidemic encephalitis of the spring of 1918 a particular cluster of symptoms was once more being singled out for scrutiny, and that here again, the epidemic so-called was merely part and parcel of a prevalence of influenza. During the last ten years evidence had been collected, however, clearly showing a close association between outbreaks of poliomyelitis, polioencephalitis, cerebrospinal meningitis and prevalences of influenza. He referred to BRORSTRÖM'S demonstration of the influenzal nature of poliomyelitis, to the London evidence relating to the common origin of cases of influenza and of cerebrospinal/

spinal fever and to the similar conclusions arrived at by Army bacteriologists from the study of the 1915 outbreak in camps.

(Dr GOODALL'S remark in the subsequent discussion to the effect that diseases which are similar are not necessarily identical seems to the reviewer to be singularly applicable to this speaker's observations).

S.P. JAMES of the Local Government Board gave a brief summary of the results of an enquiry, at the time unpublished, into encephalitis lethargica carried out by the medical staff of the L.G.B., in collaboration with the Medical Research Committee. 58 Cases had been investigated up to May 7th, from the point of view of a possible food origin with a negative result. It had been decided to adhere to the term encephalitis lethargica. Proceeding out of the enquiry it was concluded by Dr. McNALTY from his clinical study that the illness in its essential primary features had a characteristic and constant symptom series of its own and that between this symptom series and that of the rare form of poliomyelitis, with which alone it could be confused, the clinical differences were more marked than the resemblances. Epidemiologic-
al /

Epidemiological enquiries indicated too, that encephalitis lethargica was not a form of acute poliomyelitis and that its presence and epidemic prevalence, depended on conditions other than those necessary for the presence and epidemic prevalence of that disease. The speaker and Professor MARINESCO were satisfied that the present outbreak was identical with that which had been described by ECONOMO and NETTER.

A.S.MACNALTY described three types.

1. A type displaying general disturbances of the functions of the central nervous system but without localising signs.
2. Types with nervous localising signs,
 - (a) Clinical affection of the third pair of cranial nerves.
 - (b) Affection of the brain stem and bulb with local lesions of other cranial nerves.
 - (c) Affections of the long tracts
 - (d) Ataxic types
 - (e) Affections of the cerebral cortex
 - (f) Types indicating some evidence of spinal cord involvement
 - (g) Polyneuritic types.
3. Mild or abortive types with or without localising signs in the nervous system.

The incubation period was probably variable.

The prodromal period commonly ranged from one to/

to seven days, but might be as protracted as three weeks. Mild or abortive cases were rare. After-effects noted were an alteration in the mental condition, persistence of cranial nerve palsies, the subsequent appearance of paralysis apparently of spinal origin and athetosis. The suggestion was put forward by this speaker that the relationship between poliomyelitis and encephalitis lethargica might be like that between typhoid and paratyphoid.

A.J. HALL stated that he had observed 16 cases in Sheffield, not one of which had proved fatal. The epidemic began in March and was practically over by the end of April. The three cardinal signs were lethargy, general asthenia, and cranial nerve palsies. In 7 cases recovery had been complete and absolute. Recovery was practically complete in 6 cases, some slight trace of illness being left behind, while 3 cases after six months were still far from recovery.

CROOKSHANK gave statistics of 127 cases observed by him this year, 120 occurring in the London hospital. Of these, 77 were males and 50 females. 28 Cases were under five/

five years of age, 29 cases from five to ten, and 70 cases over ten. There were 26 deaths (20.39%) and 11 post-mortems had been performed. Among points worthy of note are the following:- Of 43 cases in which cytological reports of the cerebrospinal fluid were obtained, in 25 cases lymphocytes, and in 4 cases leucocytes, were found in excess. A history of injury to the head occurred in 9 cases. Sweating was noted in 13 cases, diarrhoea in 7, and constipation in 29. Glycosuria occurred (without a previous history of it) in 1 case and acetonuria in 4 cases. Vomiting occurred at the onset in 33 cases, pain in the hypochondrium in 13. Rashes occurred in 27 cases, an erythematous rash, noted in 12, being that most frequently observed. Herpes was noted in 8 cases and of these 6 were labial and 2 gluteal. Emotionalism was marked in 5 cases, delirium in 19, convulsions in 15, atrophy of limb muscle groups in 10, tenderness in the limbs in 11, and formications, tinglings and numbness were marked in 6. In 6 cases ascending paralysis occurred. (The Reviewer has only referred to certain/

certain statistical points which appear to be of interest in relation to his own observations. The impression derived from CROOK-SHANK'S statements suggest^S that the case records in the cases referred to were probably very often incomplete, and that this is the explanation of the comparative infrequency of certain symptoms which occurred in a much larger percentage of the cases related in this thesis).

47. HALL ARTHUR J. Brit.Med.Journ. Oct.26, 1918, in this paper gives in more detail an account of his experience above referred to (See reference 46).
48. BOX, CHARLES R. Lancet Nov.23, 1918, in a letter to the Lancet, refers to what he terms the "apoplectiform variety of epidemic encephalitis" which, as he indicates, is likely to be confused with cerebral haemorrhage of the ordinary type, but is mostly distinguished from this by the age incidence and by the absence of any signs of cardiovascular degeneration or chronic renal disease, while the cerebral haemorrhage of ulcerative endocarditis and of haemorrhagic blood states may be excluded by the absence of the physical signs of these diseases.

49. FARQUHAR BUZZARD, Lancet, Dec. 21, 1918, in an address upon "lethargic encephalitis" reports four cases which he regards as instances of this affection, in which the cerebral cortex was chiefly affected. All four patients were over 40 years of age, and none of them presented cardiovascular changes suggesting the possibility of cerebral haemorrhage. In all four cases the Wassermann reaction of the cerebrospinal fluid was negative.

CASE I. A female aged 54. The symptoms commenced with incontrollable jerking of the right arm and hand. A week later the whole right side was affected while there was considerable paresis and a few movements were noticed in the left arm. Later she became gradually comatose and died on May 9th, six weeks after the onset of her illness. At the post mortem a dark reddish brown staining in the subarachnoid space was evidently due to slight haemorrhage on the surface of the cortex. This was most marked over the parietal lobe on the left side, but there were small patches scattered here and there in other parts of both hemispheres. Sections of the brain presented all the characteristic appearances/

appearances of a haemorrhagic encephalitis without the occurrence of any large haemorrhage.

CASE II. A female aged 44. On May 2nd prior to which date she had, for some time, not been feeling well, weakness of the right arm was noticed. The following day, she had an epileptic attack and became more and more hemiplegic. On May 6th, there was a complete right hemiplegia. She became gradually more stuporose and was evidently suffering from increased intracranial pressure. PERCY SARGENT operated and found a great increase of intracranial pressure and a clot below the dura. Death occurred the following day. At the post mortem, the case looked like one of cerebral haemorrhage, but thrombosed veins were found on the surface of the hemisphere, and histological examination showed a widespread encephalitis.

CASE III. A male, aged 58, began to be forgetful and complain of headache while his sight became defective. On July 18th, three months later, he complained of severe headache and pains in his legs, and vomited. He was somewhat aphasic and there was a right hemianopia. The/

The temperature for two days was about 100°. The retinal veins were engorged but there was no marked neuritis. As there was no improvement Sargent operated on Aug. 1st. The intracranial tension was increased and the dura presented an appearance which suggested a slight patchy haemorrhage between its layers, while the cerebral surface was stained yellow. The convolutions were flattened and pale and here and there, there were lengths of thrombosed cortical veins. The patient gradually became more comatose and died about ten days after the operation. There was no post mortem.

CASE IV. A man aged 50, early in August fell down unconscious. His condition had been diagnosed as sunstroke. On September 13th, he was seized with very severe headache and had several epileptiform convulsions. There was a slight hemiplegia. On September 16 he died. A cerebral haemorrhage was found at the post mortem, but several portions of brain were removed by BUZZARD for microscopic examination. (A widespread encephalitis, the reviewer understands, was demonstrated, though/

though there is no note of this in the present paper.)

The above cases have been referred to in some detail, for although they are not comprised in the symptom complex described in this thesis, under the term encephalitis lethargica, it cannot be denied that they may depend upon the same virus.

50. JAMES S.P. Lancet, Dec.21. 1918. This is the summary of a paper read by the author at a recent meeting of the Royal Society of Medicine on lethargic encephalitis, (See reference 46) and refers in detail to the general and local distribution of the cases recently observed. The striking point is the wide distribution of the cases throughout England and in London.

51. CROOKSHANK, F.G., Lancet, Dec.21, 1918, At the discussion on FARQUHAR BUZZARD'S paper, speaking from the epidemiological point of view, said "they had no right to distinguish between epidemic prevalence and to say that they were due to a different disease because of difference in seasonal and age incidence".

J.G. GREENFIELD stated that positive evidence showed that poliomyelitis was a lymphogenous infection - was carried by the/

the lymph stream - whereas this was a haemato-
genous infection, the blood vessels bearing
the brunt of the disease.

FARQUHAR BUZZARD expressed the opi-
nion that poliomyelitis was an inflammation
of the nervous matter; while lethargic ence-
phalitis was an inflammation of blood vessels
with consequent effects on nervous tissues.

52. REPORT to the Local Government Board of an Enquiry
into an obscure disease, Encephalitis Lethar-
gica. This report consists of a series of
papers by Sir ARTHUR NEWSHOLME, S.P.JAMES, A.
SALLISBURY NACNALTY, G. MARINESCO, JAMES
McINTOSH, and others. Since the more impor-
tant observations and opinions of these vari-
ous observers have been already referred to,
it is not intended to make further reference
to them.